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Medical History Manuals

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PASTEUR AND AFTER PASTEUR

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LOUIS PASTEUR

Born December 27, 1822. Died September 28, 1895.

"DEUX lois contraires semblent aujourd'hui en lutte : une loi de sang et de mort qui, en imaginant chaque jour de nouveaux moyens de combat, oblige les peuples à être toujours prêts pour le champ de bataille, et une loi de paix, de travail, de salut, qui ne songe qu'à délivrer l'homme des fléaux qui l'assiègent.

"L'une ne cherche que les conquêtes violentes, l'autre que le soulagement de l'humanité. Celle-ci met une vie humaine au-dessus de toutes les victoires; celle-là sacrifierait des centaines de mille existences à l'ambition d'un seul. La loi dont nous sommes les instruments cherche même à travers le carnage à guérir les maux sanglants de cette loi de guerre. Les pansements inspirés par nos méthodes antiseptiques peuvent préserver des milliers de soldats. Laquelle de ces deux lois l'emportera sur l'autre? Dieu seul le sait. Mais ce que nous pouvons assurer, c'est que la science française se sera efforcée, en obéissant à cette loi d'humanité, de reculer les frontières de la vie."

From Pasteur's Address at the Opening of the Institute, *Nov.* 14, 1888.

PASTEUR
AND AFTER PASTEUR

BY

STEPHEN PAGET, F.R.C.S.

HON. SEC. RESEARCH DEFENCE SOCIETY

WITH EIGHT PAGE ILLUSTRATIONS

LONDON

ADAM AND CHARLES BLACK

1914

In Memoriam

LOUIS PASTEUR

BORN DECEMBER 27, 1822
DIED SEPTEMBER 28, 1895

EDITOR'S PREFACE

General history, says Gibbon, "is little more than the register of the crimes, follies, and misfortunes of mankind." In some respects this is true also as regards the history of medicine, in which a knowledge of the past may therefore conduce both to breadth of mind and to avoidance of mistakes. In these days of high specialisation, a study which exercises so broadening an effect is eminently desirable for medical practitioners.

On the other hand, it cannot be denied that in the healing art the achievements of certain individuals, and the development of periods here and there, have added immeasurably to the general virtue, wisdom, and happiness of the community; so that of late years there has been a great increase of public interest in tracing the steps by which these benefits have been secured.

For the most part, noteworthy improvements in

Medicine have arisen out of definite new discoveries in the physical sciences, have followed upon the development of fresh processes in the arts, or have been gained by the labour of outstanding individuals. The present series of Medical History Manuals has for its object to describe some of these discoveries, processes, and individuals, and to trace, in each case, the epoch that has resulted.

In this volume, Mr. Stephen Paget, F.R.C.S., has outlined the life of Pasteur, justly regarded as the founder of bacteriological methods in research, and has described many means for the prevention and expulsion of disease, which have been developed out of Pasteur's work.

J. D. C.

PREFACE

M. Vallery Radot's *Vie de Pasteur*—it has been translated into English by Mrs. Devonshire—is one of the best of all books, and ought to be in every Public Library. I have borrowed much from it; and I hope that my little book may be regarded as a sort of signpost on the way toward the well-beloved *Vie de Pasteur*.

It has been arranged to publish this manual on September 28, the day of Pasteur's death. That is a day which all physicians and surgeons—and not they alone—ought to mark in their calendars; and it falls this year with special significance for us, now that his country and ours are fighting side by side to bring back the world's peace.

S. P.

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PASTEUR AND AFTER PASTEUR

I.

EARLY YEARS OF PASTEUR'S LIFE

It is not possible to measure, or to put into words, the value of Pasteur's work and the range of his influence. All attempts to estimate or explain him are mere foolishness. Genius made his work what it was: and genius is no more the result of circumstances than a play by Shakspeare is the result of a theatre and an audience.

He was born at Dôle, in the Jura district, December 27, 1822. His father, Jean Joseph Pasteur, had served in the Peninsular War, risen from the ranks, and received the Cross of the Legion of Honour. After Fontainebleau, the regiment was disbanded; and he went back to the business of tanning, which had been in the family for two generations before him. In 1815, he married Jeanne Etiennette Roqui. He and she

were poor, but of good descent: the Pasteur family has been traced back to the seventeenth century, and the Roqui to the sixteenth—two old families of working-folk. Their first child died in infancy: then, in 1818, a daughter was born to them: in 1822, Louis, the only son: in later years, two daughters. From Dôle, the family moved to Marnoz, and thence to Arbois. Dôle is Pasteur's birthplace, Arbois was his home: a little house with a tanyard, close to the town and to the river. His boyhood was uneventful: he went to Arbois primary school, and to classes at Arbois College: he was fairly good at his lessons: and he had a talent for drawing portraits. What more should there be eighty years ago, for a poor man's child in a little French country town? But M. Romanet, the principal of Arbois College, urged him to work for a degree: and in October, 1838, he and another boy were sent to a boarding-school in Paris. The journey, forty-eight hours outside the coach in bitter weather, and the loneliness in Paris, took the heart out of him. Never was a boy, away from home, more miserable. "I should get all right," he said to the other boy, "if only I could smell the tanyard:" and the end of it was, that his father brought him back to Arbois. It was his first and last failure. In 1839, he carried off a whole armful of prizes from Arbois College: and in 1840 went

to Besançon, to the Royal College of Franche Comté. Here he studied and taught mathematics and physics, and received his board and lodging, and 300 francs a year. The spirit of hard work was upon him: and his face was set toward the Ecole Normale, the great training-college in Paris. It was at Besançon, that he and Charles Chappuis began a lifelong friendship. In 1842, he was examined for a degree in science, and passed, but without distinction; was only "moderate" in chemistry, and low on the list of candidates for the Ecole Normale: and he made up his mind to read for a year more, and then be examined again. Paris, and young Chappuis in Paris, kept calling to him: and in October, 1842, he went to Paris. He shared a room, close to his old boarding-school, with two pupils; gave lessons in mathematics, at six o'clock every morning; read hard for a degree; and attended lectures on chemistry, at the Sorbonne, by J. B. Dumas. "You cannot imagine," he writes home, "what a rush of people there is at this course. The hall is vast, and always filled. One has to go half-an-hour beforehand, to get a good place; just like the theatre. Like it, also, there is a great deal of applause. There are always six or seven hundred of us." In the summer of 1843, he did well in examination, and was fourth on the list for the Ecole Normale. His admission there determined

the whole course of his life. Henceforth, his genius was always with him.

But they who read of these early years, in M. Vallėry Radot's beautiful *Vie de Pasteur*, are apt to forget lectures and examinations, and to be thinking of the home-life at Arbois. Work hard, honour your country; put spiritual things above material, and other people before yourself; have courage, have patience: these were the precepts and the practice of the home-life. It took itself seriously: it appealed to him not for sentiment, but for grave reverence. It was poor, but not in the pinch of poverty; it was a life of work, but of skilled work; it had its high traditions, its old family names, its memories of the Army and of the Emperor, its loyalty to the Catholic Faith: it had its times of dullness and disheartenment. Here was a home that needed not only love but help, and was longing for the happiness of a great success, to make it feel young again.

His letters, from Besançon, seventy-five years ago, are more formal than the letters which we now get from youth: more solemn, more carefully worded. "Work: love one another," he writes to his little sisters. "Once you have got into the way of working, you cannot live without it. Besides, everything in this world depends on it. . . . If your resolve be strong, your task, whatever it may

be, is already begun: you have only to go on, it will accomplish itself. If by chance you stumble on your way, a hand would be there to sustain you: and, if that hand should fail you, He who took it from you would uphold you to the end." Later, he writes to his parents that he will pay for the schooling of one of the little girls: "It will be quite easy for me, by giving lessons: I have already refused to give them to several pupils at 20 and 25 francs a month: I refused because I had none too much time for my own work:" and he advises his mother not to send his sister on so many errands, but to give her more time for reading. As for himself, "Do not think that my work is making me ill. I take all the recreations necessary for my health:" and again, from Paris, "Do not trouble yourselves about my health and my work. I am taking the class because it gets me up at a quarter to six. . . . I shall spend my Thursdays in a library near here, with Chappuis: he is free for four hours on Thursdays. On Sundays, we shall walk and work together. I shall do philosophy with Chappuis on Sundays, and perhaps on Thursdays too. You can see, I am not homesick this time." Already, at Besançon, he had been old for his age, serious, devout, strong-willed, blessed with simplicity, good health, and keen enjoyment of his work. The letters from Paris

made the little house at Arbois mighty proud of him. "Tell Chappuis," his father writes to him, in December, 1834, "that I have bottled some of the 1834, bought on purpose to drink to the honour of the Ecole Normale, and that for your first vacation. There is more spirit at the bottom of these hundred litres than in all the philosophy-books in the world: but as for mathematical formulæ—faith, there are none." Arbois runs its thread all through the fabric of Pasteur's life. His mother died in 1848: his father, in 1865. Pasteur, writing from Arbois, in 1865, to his wife, says—

"... All day long, I have been remembering all the signs of my poor father's love. For thirty years, I was his constant, almost his only, thought and care. I owe everything to him. When I was young, he kept me out of bad company, and gave me the habit of work, and the example of a life absolutely loyal and incessantly occupied. This man, by nobility of spirit and of character, was high above his station, if you judge a man's station as the world judges such things. He was quite clear about that: he knew well that it is the man who makes the station, not the station which makes the man. You did not know him, dear Marie, at the time when my mother and he were working so hard for their dear children, whom they loved so much—especially for me, because my books, and the months at the College, and keeping me at Besançon, were a heavy expense. I see him still, my poor father, in such leisure as hard work

with his hands left him, incessantly educating himself; at other times, drawing, or wood-carving. It was not long ago that he was showing me a drawing of mine, in which he had put a cross: it was the only good thing in the drawing. He had a passion for knowledge and study. I have seen him studying grammars, pen in hand, comparing them, taking notes from them, just to gain, at forty or fifty years old, the learning which had been denied him by the ill-fortune of his early years."

That is the story of Arbois. But his parents did not look beyond the hope that he might obtain a professorship at Arbois College. Heaven had other designs on him. First, it gave him a thorough grounding in mathematics and physics. Then, for many years, it kept him under the discipline of chemistry. Then, for twenty years more, he was occupied over ferments, the diseases of wines, and the diseases of silkworms. He was fifty years old, when he advanced to the protective treatment of sheep, cattle, poultry, and swine, against disease: he was sixty-three, when he first used on man his protective treatment against rabies. To change the whole outlook of medicine and surgery, Heaven took and trained a "pure scientist," who had never done an operation nor written a prescription; a man who had to screw up his courage even to look at some of the ordinary sights of a hospital; took this non-medical man of

science, and set him to be head of all the heads of the medical profession, to have them all obedient to his teaching, and proud of the very sound of his beloved name. It is near twenty years since he died: and the work of these years has been done as it were in obedience to him, and in memory of him. The whole world is well aware that he has availed more than the physicians and surgeons of his time for its health and happiness. He was set apart from them, that he might be the leader of them: and he led them into that kingdom which they longed for, but could not found for themselves.

II.

CHEMISTRY

The Ecole Normale gave him his heart's desire: he was free to enjoy that magic life which makes a palace out of a roomful of books, a holiday out of a walk, and a revelation out of a lecture. There was work, and there was home: and if it was not the one with him, it was the other. In his letters home, he tells his people everything: the latest method of tanning, the fame of his teachers, and all about himself, his plans and prospects. He sends little examination-papers to his father, to help him to be more of a scholar; but filial piety devised a pretence that the papers were to be set to one of the little sisters: it is not many examination-papers that have so much love put into them. There are long letters, also, to M. Romanet, his old schoolmaster: who read them aloud to his pupils, and got Pasteur, in his vacations, to lecture to them. From 1844 to 1847, no great event crossed the line of his incessant pursuit of

chemistry; nothing more than the offer of a small appointment, and the business of submitting theses for a degree. The revolution of 1848 stirred him to enrol himself in the Garde Nationale, and to give his small savings to the cause of the Republic. "I am writing to you," he says in one of his letters home, "from the Orléans Railway, where I am on duty with the Garde Nationale. I am thankful that I was in Paris through these February days, and that I am still here. I should be sorry to leave Paris just now, with all these beautiful grand ideas unfolding themselves before my eyes. I would fight heart and soul, if need be, in the sacred cause of the Republic." A few months later, came the greatest sorrow and the greatest happiness which had yet come to him—his mother's death, and his first discovery in science: he discovered the molecular disymmetry of tartaric acid.

His study of tartaric acid and the tartrates was founded on the fact that certain crystalline substances—quartz, crystallising sugar, quinine—rotate the plane of a ray of polarised light. They retain this power, even if they be dissolved: thus, a solution of the crystals of sugar has the same action as the crystals themselves. But there are two forms of quartz: each of them belongs to the same order of crystals, each of them is quartz: for practical purposes, there is no difference between them:

but the one form rotates the plane of polarisation to the right hand, and the other rotates it to the left. Thus, there is a "right-handed" quartz, and there is a "left-handed" quartz: there is likewise a right-handed sugar, and a left-handed sugar. Furthermore, it had been observed by Haüy—it may or may not have been known to Pasteur—that these two forms of quartz-crystals. closely examined, are visibly different. Haüy had discovered, on these crystals, one very minute facet, which, before him, had not been recognised: and this facet was so placed that he could sort the crystals into two groups, according to the position of the tell-tale facet on each crystal. This difference between two forms of one crystalline substance is called disymmetry. The two forms differ, as the reflection in a mirror differs from the object in front of the mirror. They correspond, but they do not coincide. There is a pair of them: they go together: it takes both of them to make up the complete plan of the crystalline substance. And this disymmetry, which is writ large, by a tell-tale facet, on each crystal, is writ small on every one of its molecules: for, if a crystal of right-handed sugar be dissolved in water, this solution will still rotate the plane of polarisation to the right. The structure of the crystal itself is disymmetric, because the structure of each of its molecules is disymmetric:

there is disymmetry in bulk, and there is molecular disymmetry.

In October, 1844, Biot had communicated to the Académie des Sciences a note, by Mitscherlich, on the action of tartaric acid and the tartrates on polarised light. Pasteur had studied this note: and he had been shown, by Auguste Laurent, the different forms of sodium tungstate:—

"One day, M. Laurent happened to be working, if I remember rightly, at sodium tungstate—the crystals were perfect, they had been made according to the directions of another chemist, whose results he was verifying—and he showed me, under the microscope, that this salt, which looked so homogeneous, was plainly a mixture of three kinds of different crystals, which anybody fairly accustomed to crystalline forms would easily recognise. This fact, and many others of a like nature, made me understand how much might be gained, in chemistry, from a knowledge of crystalline forms. M. Delafosse, our professor of mineralogy, a man of great modesty and great distinction, had long ago taught me to love crystallography. So, to get into the way of measuring the angles of crystals, I set myself to work hard at the forms of a very fine series of compounds, which all crystallise very easily—tartaric acid and the tartrates. . . . I had another reason for making a special study of these forms. M. de la Provostaye had just published his work on them, which gave almost everything: so I could always be comparing my observations with the precise observations of an expert in physics."

Two forms of tartaric acid were known at this time. One was the ordinary commercial acid: the other was a very rare form, which had been found, by chance, in 1820, by Kestner, in the course of making the ordinary acid. Gay Lussac and Berzelius had seen and studied this rare form, and had named it paratartaric, or racemic, acid. Then, in 1844, came Mitscherlich's discovery, that the ordinary commercial acid rotated the plane of polarisation to the right: but racemic acid did not rotate it either to the right or to the left.

Thus, the problem which Pasteur had to answer may be stated as follows. "We know that a crystalline substance may be disymmetric: that it may have two forms of crystals, the one right-handed, the other left-handed. But here is a crystalline substance, having two forms of crystals: and the one of them is right-handed, but the other is neither right-handed nor left-handed. What is the meaning of that?" By careful microscopic study of the crystals of the commercial acid, he found on them a minute facet, not described either by Mitscherlich or by de la Provostaye: and this facet was so placed that he was able to feel sure that these crystals were disymmetric, one of a pair of forms: and that there must be, somewhere in Nature, the other form, the unknown acid, with a facet so placed that the two forms together would

make up the complete plan of tartaric acid. He was in quest of a left-handed tartaric acid, which Science had never seen, nor dreamed of seeing. He could only guess, that it might somehow be locked up in racemic acid.

At last, he found it. He prepared a double salt of racemic acid, a sodium ammonium racemate, and let it crystallise out: and these crystals were of two forms, one having the facet of the commercial acid, the other having the facet proper to the unknown acid. Then he separated the two forms, crystal by crystal; then, prepared two solutions, one of each form: then, tested the solutions with a polariscope: and there was the discovery. The one form rotated the plane of polarisation to the right: and the other, the form hitherto unknown to the world, turned the plane, through an equal extent, to the left. He had found the secret of racemic acid: it was itself a combination of two opposed forms: it held in itself both a right-handed and a left-handed acid. He ran out of the laboratory, fell on one of the demonstrators, and embraced him—"I've just made a great discovery; I've separated the sodium ammonium paratartrate into two salts of inverse disymmetry and inverse action on the plane of polarised light. The right-handed salt is absolutely identical with the right-handed tartrate. I'm so happy that I'm trembling

so that I can hardly put my eye to the polariscope again; let's go to the Luxembourg, I'll tell you all about it."

By this discovery, he was led to the theory that molecular disymmetry is the result of a certain grouping of the atoms of the molecule: and this theory has made its mark on the later work of organic chemistry, and on the synthetic production of drugs. Indeed, Professor Frankland writes of him as the founder of stereo-chemistry, "one of the most wonderful departments of modern chemistry." Thus, it would be possible, with a sufficient knowledge of the subject, to trace the line of descent, unbroken, from this discovery down to Ehrlich's discovery of salvarsan. That is the way, with Pasteur: his discoveries live in the work of the men who come after him.

For the next five years, from 1848 to 1853, he gave himself to the study of molecular disymmetry, with special reference to tartaric acid and its salts. In the course of this work, there was a time when the idea of disymmetry wellnigh obsessed him. It presented itself to him everywhere: all Nature moved in a disymmetrical way, her wonders to perform: life was disymmetric, the universe was disymmetric: he was experimenting with magnets to produce disymmetric crystals, and with revolving clockwork and heliostatic mirrors to produce disym-

metric substances in growing plants: he seemed wholly extravagant in this phase of Pythagorean thought. It lasted only a year or so—"One must be a bit mad," he said later, "to undertake what I did." But the records of imagination in science are full of dreams which come true: and it may be that his vision of the disymmetry of life will some day be interpreted. Meanwhile, the discovery of the left-handed acid was bringing renown to him: he was beginning to be known among men of science in Paris: and the Government made him Professor of Physics at Dijon. It was an appointment of no use to him: it took him from work of thorough originality, and set him to commonplace teaching. He did what he could: but he was longing to get away: "I can do nothing, really, here," he writes to Chappuis. "If I can't get the appointment at Besançon, I'm coming back to Paris." Happily, the appointment at Besançon, whatever it was, fell through: and he was offered the Professorship of Chemistry in Strasbourg. On January 15, 1849, he went rejoicing to Strasbourg. Friendship met him on the threshold, and Love was waiting for him just across it. Friendship was young M. Bertin, who had been at school with him, and was now Professor of Physics in Strasbourg: Love was Marie Laurent, a daughter of the Rector of the Academy. The Laurents' pure and

quiet home was like Arbois to him: and, within a month, he had sent to her father his formal proposal of marriage:—

"... My father is a tanner at Arbois, a small town in the Jura. My sisters live with him, and in the affairs of the house and of the business take the place of my mother, whom we had the grief of losing in May of last year. My family is in easy circumstances, but not rich. I estimate all that we have at not more than fifty thousand francs: and, as for me, I made up my mind long ago not to touch what will come to me, but to leave it all to my sisters. Thus, I have no private income: all that I possess is good health, good principles, and my position in the University.... As for the future, all that I can say is that, unless there should be a complete change in my tastes, I shall devote myself to researches in chemistry. My ambition is to go back to Paris when my scientific work shall have given me a reputation."

At the end of May, they were married. She was everything to him: without her, his work would never have been accomplished: he would have died, long before he did, under the strain of it. To write of him, is to be writing of her: the two lives are one, from 1849 to the day he died. His letters to Chappuis are full of happiness:—

"Why aren't you a Professor of chemistry or physics? We should be working together, and in ten years we would have revolutionised chemistry. There are marvels hidden in crystallisation: and

one day it will reveal the intimate structure of substances. If you come to Strasbourg, you'll be a chemist in spite of yourself. I shall talk to you of nothing but crystals."

Again, on October 2, 1851:

"Last Monday, I brought my year's work before the Institute. I read them a long abstract, and then I spoke, not read, a statement on some of the details of crystallography. . . . M. Dumas was almost opposite to me, and I made a point of looking at him: and he showed me, by an approving nod, that he was following me, and keenly interested. He asked me to come next morning to his house, and congratulated me. He told me, among other things, that I was a proof how, if a man in France wants to do crystallography, he knows how to do it; and that if I persevered, as he was sure I should, a school would rise out of my work. M. Biot, who is kinder to me than words can say, came to find me, after I'd read my paper, and said, 'Nothing could possibly be better.' His report on my work will be made on October 14: he seems to think that I have found a gold-mine. Don't be excited over the value of this work of mine: the credit of it comes, of course, out of my earlier work."

And again, at the end of the year:

"I think I've told you already that I was touching mysteries, and that the veil over them gets thinner and thinner. So the nights seem too long to me."

Then, in September, 1852, came that strange

episode of his life, his travelling to Leipzig, Freiberg, Vienna, Prague, in quest of racemic acid. He visited chemical factories and business houses, collected samples of tartars, learned for himself the whole process of the manufacture of commercial tartaric acid:

"I must go to the places themselves," he writes, from Leipzig, to his wife. "If I had money enough, I would go through Italy; but that is impossible: that will be for next year. I'll go on for ten years, if need be. . . . I haven't left the laboratory for three days, and all that I know of Leipzig is the street from the hotel to the University. . . . There are two tartar-refining factories at Trieste and Venice: I shall go there and examine—if I find a laboratory—their waste-products, and get to know exactly where their tartars come from. Then I shall provide myself with several kilogrammes of each kind, which I shall carefully study in France."

From Vienna, he writes to her:

"We went off to the Seybel factory, not far from Vienna. The chemist of the factory received us, and made no difficulty over letting us into the inner sanctuary: and after much questioning we came at last to feel sure that they had seen the famous acid, the racemic, last year. . . . There is another factory, in Vienna: we went there: I repeated my string of questions, M. Redtenbacher interpreting: they had seen nothing. I asked to see their products; and came across a

cask of crystallised tartaric acid, and on the surface of the crystals I could see, to my thinking, the famous stuff."

At Prague, to his amazement, he was told that they knew how to produce racemic acid; and he found that they did not, and had produced none. From Prague, he turned home, tired out. He had assured himself that racemic acid was indeed present in samples of tartaric acid from diverse countries; that it was formed in the process of refining the crude tartars; and that no chemist had ever converted pure tartaric acid into pure racemic acid. To this final task he set himself; and, after many vain attempts, succeeded, by keeping cinchonine tartrate for several hours at a high temperature. The news of this discovery was sent to Paris, and to Arbois, on June 1, 1853. Thus, in five years, the work was done, once and for all.

By the design of his life, he was always being led straight, by the very conditions which Heaven put on him, from each discovery to the next. That is what he was for. He had taken up the problems of molecular disymmetry from a purely scientific motive: he had chosen, for special study, tartaric acid, from a purely scientific motive. He had chosen—as it were at random—a grape-acid, an article of commerce, a product of fermentation: his quest of racemic acid had compelled him to see

with his own eyes the whole business of the making of wines, had carried him from crystals to ferments, from experimental physics to one of the world's most colossal industries. He has recorded how, at this time, he discovered that a racemate, in the presence of a ferment, is split up: that the ferment picks out the right-handed acid, and leaves the left-handed acid. Here, over this one observation, we seem to be standing on the very border-line between the two kingdoms, between "pure science" and "applied science." Only, his genius inspired him not to lower science to the level of trade, but to exalt trade to the level of science.

That he might have every advantage for his work in the kingdom of the industrial sciences, he must be set in a great industrial district, with manufactories all round him. This part of the design of his life was fulfilled in 1854. He was appointed Professor and Dean of the newly formed Faculty of Sciences in the University of Lille.

III.

FERMENTATION

On December 7, 1854, he gave his introductory address, in Lille, to students of technical science. He spoke in praise of science, and of theory—"Without theory, practical work becomes mere routine, by force of habit. Theory, and theory alone, can stir and develop the inventive spirit. Your business, your especial business, must be, to have nothing in common with those narrow minds which despise everything in science that has no immediate application." He took the story of Franklin, who was asked what was the use of some new fact of science, and answered, *What is the use of a baby?* And he illustrated it by Œrsted's discovery of the electric magnet, which led to telegraphy: "So it is with every theoretical discovery: its only merit is, that it exists: it bids you to hope: and that is all."

In 1855, he writes to Chappuis:

"At my fullest lectures, I have 250 or 300 men: and 21 students have put down their names

for practical work and conversation classes. . . . It is delightful to see how keen we all are: it goes so far that four of the Professors give their written lectures, revised by themselves, to a printer, who types them: he has already 120 subscribers for the course on applied mechanics, and is printing 400 copies. . . . I have what I always longed for, a laboratory where I can go at all hours, on the floor below my own room: and sometimes, while I sleep—often, these days—the gas is burning all night, and the processes are going on of themselves. . . . Add to all this, that I belong to two very active societies, and that I've been appointed, by the General Council, to test fertilisers for the Department of the North: rather a heavy job, in this rich agricultural country, but I took it gladly, to popularise and extend the influence of our new Faculty. Don't be afraid that it will all divert me from my beloved researches. I shall not give up them. . . . Let's all work: there's no amusement like work: that is what Biot used to say, and he is an authority on this point."

Beside lecturing, he would take students over foundries and factories: and, in 1856, he took them for a tour in Belgium, to see something of Belgian industries. But the problems of fermentation were always before him. In 1856, he was at work over the manufacture of alcohol out of beet-sugar: in 1857, he gave to the Lille Scientific Society his paper on the lactic-acid fermentation. He had discovered, in sour milk, a trace of a greyish substance; had proved it to be indeed a ferment of

milk; had isolated this *bacterium lactis*, had sown it on milk, and seen it act. If we care for that ill-treated phrase, *An epoch-making discovery*, here is an occasion for its use. It fixes the date of the birth of the New Learning.

Paris, this memorable year, claimed him back from Lille: he was appointed in charge of the science-teaching of the Ecole Normale, and of its general management; and a laboratory was assigned to him, but miserably small and ill-furnished—a mere garret in the Rue d'Ulm: but he made it serve, and that for work as revolutionary as any ever accomplished in science. He was studying fermentation, off and on, for twenty years or more. How is it possible to describe, in a page or two, the output of these twenty years, the changes which they wrought in the manufacture of wines, vinegars, and beers? The incessant use of the microscope, the adaptation of processes to the individual ways of each ferment, the proper sterilisation of apparatus—these were the principles of his teaching. In 1868, he taught France how to keep her rough wines from going sour, by warming them, in the vat, at a certain point of fermentation: in 1867, he taught the vinegar-makers of Orleans how to speed-up the fermenting vinegar: in 1871, in London, he took by surprise a huge East-End brewery, proving to them, with his microscope, the

impurity of their yeast, and the evil result on the liquor. Always, he is the man with the microscope: he understands the nature and the life-history of each ferment: its range of action, its tricks and its ways, what it likes, what it dislikes. For the diseases of wines, his was the best opinion: there was none so well able, from the look of a speck of yeast or a film of sediment under the microscope, to give a correct diagnosis and a correct prognosis. No man has done more to raise brewing and wine-making to their present standard of accuracy and of purity. Not that he stands alone, or that no further advance has been gained since his time: there is the work of Hansen, Traube, Nägeli, Buchner, Jacobsen, and many more: there are new methods, new safeguards, new forms of yeasts identified and classified, new exercises of theory in chemistry. The controversy, fifty years ago, between Liebig and Pasteur—between the older man of science, who thought of fermentation in terms of molecular physics, and the younger man of science, who thought of it in terms of plant physiology—has been resolved by Buchner's work: who, in 1897, extracted from yeast the very substance of its ferment, the zymaze, separable from the yeast-cells, yet formed within them, as ptyalin is formed within the cells of the salivary glands. The action of zymaze may be stated in terms of molecular physics:

the formation of zymaze may be stated in terms of plant physiology: thus, the old lines of dispute are left behind.

Again, a wonderful advance was made, in 1879, by Hansen's method of marking-down, in a thin film of a very dilute mixture of yeast and water, under the microscope, single cells, and then, when these cells began to form colonies visible to the unaided eye, making cultures from these colonies, and thus obtaining a yeast of absolute purity and of known pedigree. It seems that honours are even between Pasteur and Hansen: from 1880, it is Hansen; before Hansen, it is Pasteur.

Only, to him, vast industries presented themselves chiefly as hunting-grounds of science: they were "parts of one stupendous whole": he was at work not only to improve the world's beverages—though he was glad to do that, for the honour and glory of France—but to prove that all processes of fermentation, decomposition, and putrefaction, are infective processes: that they are due, not to the oxygen in the air, but to the living dust in the air: that they are an act of life, and cannot begin apart from life. It is life which brings about these chemical changes: and, in the absence of life, they do not take place. These microscopic points of life, these yeasts and bacteria, millions of them in a drop or two of fermenting grape-juice, sour milk,

or putrid broth, can be filtered out from the air, leaving it sterile: and, in air thus sterilised, no liquid will ferment or putrefy.

By 1859—the year of publication of *The Origin of Species*—Pasteur was in the thick of the fight over the Origin of Life. Was it possible for bacteria to come of themselves, or was it not? If, in a flask of broth, supposed to be sterilised, they made their appearance, and the broth went bad, was it absolutely certain that they had got in from outside? Was it not possible that they had been spontaneously generated in the broth? Must all life, even lives so minute as these, be the work of life? Surely, life must begin somewhere: why not here, struck out of air and broth like sparks out of steel and flint? Long ago, men had ceased to believe in the spontaneous generation of grubs, maggots, tape-worms, and so forth: but these ultimate invisible particles, these mere beginnings, might they not be too small to be included under the law, *Omne vivum ex vivo?* Besides, it is a pleasant creed that life is always coming of itself, emerging out of not-life, as Aphrodite came of herself out of the foam of the sea.

He set himself to the hard business of proving a negative. Among his opponents, the most notable were Pouchet and Joly. In England, the controversy was between Tyndall and Bastian. It

took hold on public thought: for all are interested in Life, and some are apt to think that Science is in a position to say what Life is. Pasteur would not philosophise: he went straight to work. His innumerable experiments with filtered air, heated air, and organic fluids—milk, broth, urine, blood—and his use of air-filtering flasks, and his comparative observations on air at the level of the streets and air above the snow-level, were repeated by his opponents: and, now and then, one or more of their flasks would show the presence of life, and the controversy would start all over again. The whole conception, half a century ago, of putrefactive bacteria, was unfamiliar to Science: he had to feel every inch of his way: he had not the tests, the instruments, the culture-media, which to-day are in every laboratory: the wonder is, not that the controversy endured so long, but that it came to an end so soon. By 1865, it was over: there is still one lingering note of it to be heard: but Pasteur and Tyndall, for all that, had won all along the line. Two years ago, at the meeting of the British Association in Dundee, Sir Edward Schäfer, in his Presidential Address, lifted the thought of the Origin of Life to its very highest place in scientific theory. He rather affirmed than denied that Life may have come of itself, and may still be coming of itself: but he was none the less sure of the everlasting veracity of Pasteur's work:—

"I am myself so entirely convinced of the accuracy of the results which Pasteur obtained—are they not within the daily and hourly experience of everyone who deals with the sterilisation of organic liquids?—that I do not hesitate to believe, if living *torulæ* or *mycelia* are exhibited to me in flasks which had been subjected to prolonged boiling after being hermetically sealed, that there has been some fallacy either in the premisses or in the carrying out of the operation. . . . If the formation of life, of living substance, is possible at the present day—and for my own part I see no reason to doubt it—a boiled infusion of organic matter, and still less of inorganic matter, is the last place in which to look for it."

That is "the germ-theory." It is not a philosophical theory of life, but a most practical doctrine, that fermentation, decomposition, putrefaction, are the act of the living dust of the air: that these bacteria are not begotten by the fermenting liquid, but come into it from outside: that a liquid, really sterile, exposed to air really sterile, will remain sterile for ever. Out of the many episodes of the fight, take Pasteur's famous lecture, at the Sorbonne, April 7, 1864. All Paris was there: the huge amphitheatre was filled to overflowing: he showed them his flasks, his sterilised broth: he told them the history of the controversy, told it with quiet grave conviction, and just a little touch of scorn for his adversaries—"There is no condi-

tion known to-day in which you can affirm that microscopic beings come into the world without germs, without parents like themselves. They who allege it have been the sport of illusions, of ill-made experiments, vitiated by errors which they have not been able to perceive, and have not known how to avoid." He described himself, in a passage of singular beauty, watching his flasks, imploring them to give him a sign of life, and they would not —"for I have kept from them, and am still keeping from them, that one thing which is above the power of man to make; I have kept from them the germs which float in the air, I have kept from them life." And he proclaimed "the germ-theory"—proclaimed it, surely, in the shortest words to be had—*La vie c'est le germe et le germe c'est la vie.*

But the germ-theory began to be born not in 1864 but in 1857, of his work on the lactic-acid fermentation: and that work is inseparable from the rest of his work at Lille. Never is he at work on brewing and wine-making alone, for their own sake: always, his mind is set toward the whole kingdom of life in the air. He improves the ways of vinegar-factories and wine-factories, he enriches France, and other countries, year in year out: but the vision before his eyes, the whole time, is of nothing less than a true understanding of all

infection. So early as March, 1863, when he was presented by J. B. Dumas to Napoleon III., he told the Emperor that his one ambition was to get to know the causes of putrid and contagious diseases. So early as 1862, he published a note on the presence of certain germs in ammoniacal urine, such as are present in disease of the bladder. So early as November, 1860, writing of his experiments at Chamonix on the sterility of air above the snow-level, "What is wanted," he said, "is to extend these observations far enough to prepare the way for a thorough study of the origin of different diseases."

We are so full, nowadays, of germ-facts, that we have left off talking of "the germ-theory." It is just half a century, since he demonstrated his method to all Paris: we must put ourselves back fifty years, to 1864. We must note the one thought which dominated the germ-theory. It was the thought of putrefaction. Broth, infected by the living dust of the air, goes bad, stinks, becomes putrid. The germs which have got into it are the germs of putrefaction. Do away with these germs, keep them out or kill them off, and you will prevent putrefaction. That was the teaching of the germ-theory, in 1864. Then, in 1865, came Lister's first use of carbolic acid to prevent putrefaction in a case of compound fracture.

IV.

PASTEUR AND LISTER

In 1865, Lister was thirty-eight years old. From Edinburgh, where he had been an assistant-surgeon to the Royal Infirmary, and an extra-mural lecturer on Surgery, he had gone, in 1860, to Glasgow, to be a surgeon at the Royal Infirmary, and Professor of Surgery in the University. By 1865, he had done an immense amount of scientific work on the subject of inflammation: he had contributed, to the Philosophical Transactions of the Royal Society, in 1858, a long paper *On the Early Stages of Inflammation:* and, in 1863, he had given the Croonian Lecture, *On the Coagulation of the Blood.* He became a Fellow of the Royal Society at the early age of thirty-two.

It would be useless to put here a long account of the misery and peril of compound fractures, wounds, operation-cases, and maternity-cases, in the years before "Listerism" came into general use. Those of us who are old need not be reminded of it: and

Elliott & Fry, Ltd.

Yours very truly
Lister

those of us who are young saw nothing of it. The tragedy is too great for words: it was the burden of all military surgery, all hospital and private practice, all midwifery, in every city on earth, for centuries. Pyæmia, septicæmia, erysipelas, cellulitis, hospital gangrene—it is nothing, to write the names: but it is enough, here, to write them: we have only to note that these infections were scourging the Glasgow Infirmary, to their hearts' content, right up to 1865, as they were scourging other hospitals in all countries; and were called—one writes the most evil-sounding of all the names—hospital diseases.

From 1860 to 1865, as we look back, it is evident—if the phrase may be pardoned—that something was bound to happen very soon. Trousseau and Chalvet and Lemaire in France, Lund and William Budd and Spencer Wells in England, these and others were possessed of the significance of Pasteur's work. Preparations of creasote, for the cleansing and dressing of wounds, had long been in use. To read Lemaire's monographs, *Du Coal-tar Saponiné*, 1860, and *De L'Acide Phénique*, 1863, and Spencer Wells's address at the Cambridge meeting of the British Medical Association, 1864, is to realise that everything was ready for Lister's work.

We say that he discovered the antiseptic method: but we must not think of any sudden invention of

"modern surgery." It took him years of incessant study, to do what he did for the world. His accounts of his work are well known to all students of his life: it will suffice to quote the famous passage in his Presidential Address to the British Association, in Liverpool, in 1896:—

"Nothing was formerly more striking in surgical experience than the difference in the behaviour of injuries according to whether the skin was implicated or not. Thus, if the bones of the leg were broken and the skin remained intact, the surgeon applied the necessary apparatus without any other anxiety than that of maintaining a good position of the fragments, although the internal injury to bones and soft parts might be very severe. If, on the other hand, a wound of the skin were present communicating with the broken bones, although the damage might be in other respects comparatively slight, the compound fracture, as it was termed, was one of the most dangerous accidents that could happen. Mr. Syme, who was, I believe, the safest surgeon of his time, once told me that he was inclined to think that it would be, on the whole, better if all compound fractures of the leg were subjected to amputation, without any attempt to save the limb. What was the cause of this astonishing difference? It was clearly in some way due to the exposure of the injured parts to the external world. One obvious effect of such exposure was indicated by the odour of the discharge, which showed that the blood in the wound had undergone putrefactive change by which the bland nutrient liquid had been converted into

highly irritant and poisonous substances. I have seen a man with compound fracture of the leg die within two days of the accident, as plainly poisoned by the products of putrefaction as if he had taken a fatal dose of some potent toxic drug. . . .

"These and many other considerations had long impressed me with the greatness of the evil of putrefaction in surgery. I had done my best to mitigate it by scrupulous ordinary cleanliness and the use of various deodorant lotions.* But to prevent it altogether appeared hopeless while we believed with Liebig that its primary cause was the atmospheric oxygen which, in accordance with the researches of Graham, could not fail to be perpetually diffused through the porous dressings which were used to absorb the blood discharged from the wound. But when Pasteur had shown that putrefaction was a fermentation caused by the growth of microbes, and that these could not arise *de novo* in the decomposable substance, the problem assumed a more hopeful aspect. If the wound could be treated with some substance which, without doing too serious mischief to the human tissues, would kill the microbes already contained in it and prevent the future access of others in the living

* "I freely used antiseptic washes, and I had on the tables of my wards piles of clean towels to be used for drying my hands and those of my assistants after washing them, as I insisted should invariably be done in passing from one dressing to another. But all my efforts proved abortive, as I could hardly wonder when I believed, with chemists generally, that putrefaction was caused by the oxygen of the air. It will thus be seen that I was prepared to welcome Pasteur's demonstration that putrefaction, like other true fermentations, is caused by microbes growing in the putrescible substance."—*Huxley Lecture*, 1900.

state, putrefaction might be prevented, however freely the air with its oxygen might enter."

That was the problem, half a century ago: how to prevent putrefaction in open wounds. Pasteur could prevent putrefaction in broth, by his aseptic method: but patients cannot be boiled, nor kept in filtered air, in flasks. Here is a man, with a dirty lacerated wound, already tenanted by the germs of putrefaction, got into it from outside: what must be done for him? This must be done: the germs must be killed, and no more must be allowed to get into the wound. To kill the germs in the wound, Lister chose undiluted carbolic acid:* to

* "The crude carbolic acid which, under the name of German creasote, was supplied to me by my colleague, Dr. Anderson, Professor of Chemistry in the University of Glasgow, was a brown liquid which had been adulterated with water." (*Letter from Lord Lister to Sir Hector Cameron in* 1906.) Creasote came into public use, about 1840, as a preservative of wood. A few years later, came the use of disinfectant powders containing coal-tar. Lemaire's first preparation of carbolic acid (August, 1859) was an emulsion of coal-tar in alcoholic tincture of saponine: a few months later, he got some more or less pure carbolic acid specially made for him. Pure carbolic acid, he says, was discovered, in science, by Runge, in 1834, and was so named by him: Laurent called it phenic acid: Gerhardt called it phenol. For a quarter of a century or more, it was nothing more than a rare product of chemistry. "Il est certain qu'à la fin de 1859 on ne trouvait pas d'acide phénique dans le commerce; mes premières expériences ont été faites avec une petite quantité que je devais à l'obligeance de M. Dussard. Il était liquide. Depuis, j'en ai fait demander chez presque tous les fabricants de produits chimiques de Paris. Ils n'en avaient

prevent any more germs from getting in, he left untouched the scab or crust formed by the acid and blood together on the wound. His first case, in March, 1865, failed: his next case, in August, was successful. He felt his way, with profound care and watchfulness, from case to case: venturing, when he dared, to modify his first method. Over case 5, a child run over by an omnibus, he fought for six months to save the limb: and saved it. Over case 8, he used not the undiluted acid, but 1 part of the acid to 3 of olive oil. Over case 9, as there was not enough blood in the wound to form a crust, he used a paste of starch and acid. In 1867, he published, in the *Lancet*, his eleven

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pas. J'ai été obligé d'en faire préparer exprès deux kilogrammes avec lesquels j'ai fait toutes mes expériences."—*De l'Acide Phénique*, 1863. The date of Dr. Crace Calvert's work on carbolic acid is 1862. Lister, of course, never claimed priority in the use of carbolic acid. He had chosen it because he knew of its "remarkable effects upon the sewage of the town of Carlisle: the admixture of a very small proportion not only preventing all odour from the lands irrigated with the refuse material, but, as it was stated, destroying the entozoa which usually infest cattle fed upon such pastures." Again, he never claimed that the acid had any specific effects on the germs of putrefaction, such as quinine has on malaria, or salvarsan on syphilis. Thus, in 1868, he wrote: "So far from carbolic acid being a specific, it owes its virtues to properties which it possesses in common with various other substances; and results similar in kind to those obtained by its means might be got by disinfectants long familiar to British surgery, provided always that the same principles guided their employment."

cases of compound fracture, with a "preliminary note" on the antiseptic method of opening abscesses: the title of this paper is *A New Method of Treating Compound Fracture, Abscess, etc.: with Observations on the Condition of Suppuration.* For the opening of abscesses, he guarded his incision under a veil of carbolised rag, and used a carbolised knife, dropping the veil over the incision as he withdrew his knife: the matter flowed out from under the veil: the dressing was a paste or putty of carbolic acid in oil, with common whitening, spread on block-tin, and kept in place with adhesive plaster; the lower edge of the dressing was left free, so that the discharge might escape into a folded towel bandaged over the dressing. By this method of the antiseptic veil and putty, he prevented the entry of germs from the air into the opened cavity of the abscess; and thus enabled the cavity to close of itself, by antiseptic drainage. In 1867, at the Dublin meeting of the British Association, he spoke of the value of his method, not only for cases of injury, but for cases of operation:—

"If the severest forms of contused and lacerated wounds heal thus kindly under the antiseptic treatment, it is obvious that its application to simple incised wounds must be merely a matter of detail. I have devoted a good deal of attention to this class, but I have not as yet pleased myself altogether with any of the methods I have employed. I am, how-

ever, prepared to go so far as to say that a solution of carbolic acid in twenty parts of water, while a mild and cleanly application, may be relied on for destroying any septic germs that may fall upon the wound during the performance of an operation; and also that for preventing the subsequent introduction of others, the paste above described, applied as for compound fractures, gives excellent results. . . . Further, I have found that when the antiseptic treatment is efficiently conducted, ligatures may be safely cut short and left to be disposed of by absorption or otherwise."

On December 12, 1867, he made his experiment with a carbolised silk ligature, tied in continuity round the carotid artery of a horse: on January 30, 1868, he used a similar ligature for a case of femoral aneurysm. On December 31, 1868, he made his experiment with a carbolised ligature of animal tissue, tied in continuity round the carotid artery of a calf. Later, he introduced the use of dressings of antiseptic gauze.

These crowded years of laborious work refuse to be contained in a few lines of print. He was incessantly watching, judging himself, proving in science every point of practice, repeating for himself many of Pasteur's experiments, advancing, inch by inch, with profound anxiety lest he should be endangering a life or a limb. There never was, nor ever will be, a surgeon more careful over

each case, more open-minded in his criticism of his own method.

We are too apt to think of "Listerism" as a set of rules for the safe performance of operations. That is not how it was discovered. It was, first and foremost, a way of preventing putrefaction in compound fractures. And we are too apt to talk as if "the aseptic method of operating"—the sterilising, by heat, of instruments, dressings, towels, and so forth—had somehow taken the meaning out of Lister's work. That is not how the science and art of surgery, or any other science and art, are improved. Putrefaction, scourging the wards of the infirmary, killing case after case with pyæmia or with hospital gangrene—that was what Lister had to fight, and fought, and beat. And if A, B, or C, to-morrow, were to be run over, and be admitted to hospital, with a smashed leg, and germs all ground into the wound, he or she would have the advantage of "Listerian precautions," as they used to be called. Indeed, antiseptic and aseptic are nothing more than two ways of arriving at one result; two lines of attack against one enemy. As Sir William Osler said to the Royal Commission on Vivisection, on November 20, 1907, "It is the difference between tweedledum and tweedledee. They are both applications of the same principle." For example, neither catgut

ligatures, nor the surgeon's hands, nor the patient's skin, lend themselves to be sterilised by heat. It is true, that Lister was more afraid of the powers of the air, half a century ago, than surgeons are now: it is true that his use of a carbolic spray, to sterilise the air round the wound, has been given up *: but the law of all operations remains to-day

* Sir Hector Cameron, his house-surgeon at the Glasgow Infirmary, and his life-long friend, writes of him: "After he had gone to Edinburgh (1870) he began the use of a carbolic acid spray, during operation and the subsequent dressings of the wound, with the object of displacing the surrounding atmosphere and substituting for it one charged with a finely-divided germicidal solution. Later experience, and the growth of bacteriological knowledge, convinced him, in after years, that such precautions were not really necessary: and he 'was led to conclude that it was the grosser forms of septic mischief, rather than microbes in the attenuated form in which they existed in the atmosphere, that we had to dread in surgical practice.' He had hinted, at the London Medical Congress in 1881, when describing some bacteriological experiments which he had carried out, that it might yet be possible to disregard the atmosphere. It was not, however, until the Berlin Congress in 1890 that he was able to bring forward what he considered absolute demonstration of the harmlessness of this supposed source of infection, and to announce that he felt himself justified in abandoning the use of the spray . . . I refer to this matter in some detail because I often hear people speak as if, at this early period of his work, infection of the wound by the atmosphere was the only source of defilement against which he took precautions. Nothing could be further from the truth. If he did guard against that supposed source of danger with an unnecessarily constant and watchful rigour, he was equally insistent, from the first, upon the careful sterilising, by means of carbolic acid solution, of all hands coming directly or indirectly into contact with the wound; as well as the skin

that law which was revealed to him in 1865, in the light of Pasteur's work on putrefaction. From the very first, antiseptic surgery had in itself the makings of aseptic surgery.

Saxtorph, Lucas-Championnière, von Nussbaum, von Volkmann, von Billroth—these names come first to be remembered, of the great surgeons in other countries, who were quick to see the truth of his doctrine. In our own country, there was more than enough of controversy: but it is easy to see why he was criticised, even by men of good common sense. To some of them, the work of Pasteur seemed no more than a theory: yet, to believe in Lister, you must believe in Pasteur. To some, the very notion of dressing wounds with "putty" gave offence. And there was a host of other arguments: that Listerism prolonged the operation, tempted men to be bold in excess of their manual skill, or made them forget the constitution of the patient; that cases had occurred of carbolic-acid poisoning; that good results, as good as Lister's, had been got with half-Listerism, or with non-Listerism; that you could not separate the credit due to him from the credit due to better nursing, better house-surgeons, less purging, less

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of the patient widely around the situation of the intended operation, and all sponges, sutures, ligatures, and instruments about to be used."—*Brit. Med. Journ.*, December 13, 1902.

mercury, less brandy; and so forth. Even so late as 1877, when he came from Edinburgh to London to be Professor of Surgery at King's College, it was still to be criticised, for a few years more. He kept himself from all wasteful talking and writing: he gave himself, body and soul, to the perfecting, in science and in practice, of surgery. Slowly, in Glasgow, in Edinburgh, in London, he thought out, proved, and made known this or that new operation, this or that new device: the chromicised ligature, the sal-alembroth and cyanide gauzes. In 1893, the death of Lady Lister—they had no children—took the light out of his life. The whole world was honouring him: no man of science has ever had more love, more worship: for nineteen years, she was not there to be pleased with it all. The sense of loneliness deepened in him, through the later years. He died on February 10, 1912. To recall him, is to think, first, of the dignity, gentleness, and refinement of his face: its delicate colouring, the tranquil, almost dreaming, look of his eyes: the lines of the mouth were soft, and might even be considered weak by those observers of mankind who admire thin, tight-lipped faces: there was none of the tragical and sombre intensity which was in Pasteur's face: but a wonderfully quiet, wise, and kind expression. His voice was soft, and free from self-consciousness, and almost

with a touch of irresoluteness: not the voice of a man who cared for arguments and speech-making. He had been brought up in the Society of Friends: and his peaceful face and voice revealed the peace of his spiritual life. He held on like iron to his purposes: but he did not look so masterful as he was. He smiled, not laughed: a smile of singular beauty, but hard to interpret in all its bearings: yet it was far more eloquent, or more disconcerting, than the average man's laughter. Mostly, he looked tired: not tired of science and practice, but tired of being told that every country of the world was thankful for his work; that he had saved more lives than the armies of Napoleon had destroyed; that all mankind was daily and everlastingly grateful to him. Tired, lonely, and, long before he died, broken in health and in the enjoyment of living, one thinks of him, still, as a man serene through controversy, a spirit of invincible patience and of radiant purity.

V.

DISEASES OF SILKWORMS

It was in March, 1863, that Pasteur told Napoleon III. that his one ambition was "to discover the causes of putrid and contagious diseases." In the autumn of 1865, the cholera came from Marseilles to Paris: in October, there were more than 200 cases a day: and Pasteur, Claude Bernard, and Deville, made many experiments on the air of a cholera-ward in the Lariboisière Hospital.* In 1865, also, Pasteur took up the study of the silk-worm disease. For near twenty years, the silk industry had been going from bad to worse: France, Italy, Spain, Greece, Turkey, China, were all involved: the loss and the misery, down in the South of France, were terrible: it needed only a few more turns of the screw to squeeze the life out of this great national industry. He set his

* "Un jour que Henri Sainte-Claire Deville disait à Pasteur, 'Il faut du courage pour ce genre d'études,' *Et le devoir?* lui dit simplement Pasteur. Le ton donné à ce mot *devoir*, racontait Sainte-Claire Deville, valait tout un enseignement."—*Vie de Pasteur*, chap. vi.

hand to the work, this chemist who had never touched a silkworm; he discovered the cause and course of the disease, and the way to prevent its recurrence; he brought back prosperity to the silk trade, and saved his country out of her distress. It was one of the hardest of all his studies: and it was a time of bitter sorrow for him. In June, 1865, his father died: in September, his child Camille: in May, 1866, his child Cécile: in October, 1868, he suffered a cerebral hæmorrhage, and nearly died: in 1870, came the Franco-German War. The difficulties of the work, even to-day, would be formidable, if a man were to start investigating the disease, with all the latest advantages to help him. In 1865, the difficulties were ten times greater: no such investigation had ever yet been made: every inch of the way had to be cut, like steps in ice. Besides, he had to deal with a full measure of opposition, prejudice, and downright dishonesty. These years, which began with the wrecking of his home and ended with the wrecking of his country, were indeed heavy and full of grief: but, in the end, he won. Nothing, in the later years of his life, surpasses his *Études sur les Maladies des Vers à Soie.* He used to commend this book to students: and there could hardly be a better guide for young men of science.

The disease was called *pébrine,* from the black

spots, like pepper, which came on infected worms. Tons of all sorts of remedies—disinfection, fumigation, and so forth—had been tried, in vain, season after season. Things looked utterly hopeless. Sometimes the worms would sicken early, sometimes they would sicken late; sometimes they would seem healthy right up to the period of spinning, yet the moths would be unhealthy, and the disease would recur in the next year's worms. Theories of the disease were to be had in any number. One or two microscopists had found, in the worm or in the moth, certain oval "corpuscles": but had stopped there, making nothing of them.

On June 6, 1865, Pasteur started for Alais, a hot-bed of the disease. By incessant questioning, he was able to measure the bewilderment of the proprietors: they had tried everything, thought of everything, accomplished nothing. He set himself to find out the meaning of the corpuscles. At once, he was in the thick of perplexities. He had under examination two lots of worms: we may call them A and B. Both were raised from Japanese seed: lot A was from seed officially guaranteed: lot B was not guaranteed. Lot A spun well: lot B languished. But he found only a few corpuscles in lot B: and he found many in the chrysalids and moths of lot A. He waited till lot B had spun: and he found that the chrysalids

and moths contained many corpuscles. From these facts, viewed in the light of his theory that the corpuscles were indeed the cause of the disease, he inferred that the disease had its chief development in the chrysalid and the moth. If the moths were heavily infected, next year's worms would early show signs of the disease: if the moths were slightly infected, next year's worms would only some of them show signs of the disease, and that late, not early. He compared it to the children of phthisical parents: some of the children will suffer slightly and late, others will suffer heavily and early.

In February, 1866, he returned from Paris to Alais, with two assistants: they took a house at Pont Gisquet, fitted up a laboratory, and worked incessantly. In June, he writes to his friend Duruy, the Minister of Public Instruction, telling him of the little Cécile's death—

"Here I am, back again, heart and soul, at my work, the one thing which takes me off such a sorrow as mine. . . . I shall be in a position, when I come back, to propose to the Commission on Silk-culture a practical way of fighting the evil, and of making it disappear in a few years. . . . My observations show that it develops principally in the chrysalid, and, above all, in the mature chrysalid, that is, at the moment of the formation of the moth, on the verge of the function

of reproduction. At that stage, the microscope shows it with absolute certainty, even if the seed and the worms appeared very healthy. The practical result is—You have a roomful of silkworms: it has done well, or ill, or fairly well: you want to know whether to steam the cocoons and send them to be unwound, or keep them for reproduction. Nothing easier. Raise their temperature, hasten the coming out of a hundred or so of the moths, examine them under the microscope: that will tell you what to do. And the thing is so easy to recognise that a woman or a child could be trusted with it. I admit that the seeding may be in the hands of some countryman, with no chance of his settling the point then and there: but, instead of throwing away the moths after mating and laying, he can put a large number of them, just as they happen to come, in a bottle half full of spirit, and send them to a research bureau, or to some man of experience: and thus we should have a whole year, if we wanted it, to judge the worth of the seed which will have to be taken in hand next spring."

It was in 1866, also, that he proved the contagiousness of the disease, by feeding worms on mulberry-leaves smeared with the corpuscles.

In January, 1867, he was again at Alais, with his assistants, and with Madame Pasteur and his only daughter. He quickened—a mere matter of temperature—the hatching of last year's seed: he found his prophecies coming true. He used to begin work at dawn, and work all day. Then came his discovery of other ways of contagion,

beside that of infected leaves. A trayful of healthy worms could be infected by the droppings from a trayful of diseased worms put above them: and diseased worms, put among healthy worms, could infect them. On March 1, in a letter full of hope, he is impatient over the general belief that the country folk could not use a microscope—"Don't tell me that anybody wants anything simpler than a preventive method which is just to put your eye to the eye-piece of a microscope after pounding a moth in a mortar with a few drops of water—mere child's-play, taking an hour or two to learn. A deadlock here would be absurd, especially when you think how we are dealing with a state of things which means to France, let alone other countries, the loss of 30, 40, or 50 million francs a year, and to each proprietor the loss of his chief, often his only, income."

Then came another set of problems. Another disease, called *morts-flats* or *flacherie*, broke out among his worms: he had now to labour not over one disease, but over two. *Flacherie* may be defined as a septic disease of silkworms, due to the eating of leaves contaminated by the specific germs of the disease: leaves sodden with rain, or unclean with dust, are apt to be thus contaminated. The germs of *flacherie* are found in the digestive canal of the worm, and in the stomach-pouch of the

chrysalid and the moth: and may infect the seed. To prevent this disaster, it suffices to hasten up, by warmth, some of the moths, and examine under the microscope a particle of the stomach-pouch. If *flacherie* be found in them, all the seed from that brood must be destroyed, lest it spread the disease. By 1868, Pasteur had worked out these facts. His coming to Alais, that year, was in triumph: his prophecies were fulfilled, as in 1867, so in 1868: henceforth, the way was clear to all men, how to protect this great international industry and bring back the good times. Back in Paris, he was occupied over problems of fermentation. On October 19, he suffered a cerebral hæmorrhage. It is a memorable story that M. Gernez, one of his assistants at Alais, tells of this illness—"One night when I was alone with him, I had been trying in vain to divert him from these thoughts (of his unfinished work). At last, I gave up hope of succeeding, and let him think-out the ideas which he was wishing to make known. Then, finding, to my astonishment, that they had the clear and precise form which all his work has, I wrote at his dictation, without changing a word, and took next morning to his illustrious colleague Dumas, who did not believe his eyes, the note which appeared in the *compte rendu* of the Academy, October 26, 1868. This was eight days after the seizure which

had nearly carried him off. It was an outline of a most ingenious method for detecting, by hastening the production of a series of seeds, which of them were predisposed to *flacherie*."

Other events, in 1868, were the publication of his appeal to France to do more for Science; the conference, on this matter, between the Emperor, Pasteur, Claude Bernard, Duruy, and others; the final proof, at Brest, Toulon, and elsewhere, of his method of keeping rough wines from souring; and the rebuilding of the laboratories in the Rue d'Ulm.

In January, 1869, he insisted on getting back near Alais: long before he was well. In February, he dictates a letter to J. B. Dumas: he is doing what work they will let him: the demands for non-infected seed are so heavy that he cannot meet them. The Lyon Silk-Commission think his method valuable, but his results not absolute. *They are absolute*, he answers; and he sends them four lots of seed. Watch these four lots, he tells them: one shall succeed: one shall die of *pébrine* only: one shall die of *flacherie* only: one shall die part of *pébrine* and part of *flacherie*. And so they did. A proprietress is distributing samples of seed far and wide, sure of their healthiness: the Minister of Agriculture asks Pasteur's judgment on them, sends him three lots: "These three lots of seed,"

he writes back, "are detestable. I have thrown them into the river." The good lady was spreading *pébrine* broadcast.

He had still to make an end of all prejudice, falsehood, and tricks of the trade: let there be—*Oh, the crowd must have emphatic warrant*—one final manifestation of the value of his method, for everybody to see and accept. In November, 1869, the Emperor lent him Villa Vicentina, a great estate, not far from Trieste, belonging to the Prince Imperial. On November 25, Pasteur went there from Alais, with 100 ounces of selected seed. For ten years, the silk-industry of the estate had been wrecked by *flacherie* and *pébrine*. He spent the winter there, recovering his strength, writing the two volumes of his *Études sur les Maladies des Vers à Soie*, and preparing for the spring: and he had need to be on the watch, for he caught a man on the estate selling suspected seed, from Japan, to be mixed with the Alais seed. The cocoons off the estate, in 1870, gave a clear profit of 22,000 francs: the first penny of profit made for ten years. Then, within a few days after this triumph at Villa Vicentina, came the Franco-German War.

That is the story of Pasteur's life up to 1870. He had helped to discover a new department of chemistry: he had revolutionised the manufacture

of wines and vinegars: he had proved the truth of the germ-theory: he had founded, with Lister, the methods of modern surgery: and he had been the very saving of the silk-trade. It is only a few weeks ago, at Le Muy, near St. Raphael, that I went over a silkworm nursery, and found his methods in use, as in 1870, so in 1914. *Flacherie*, I was told, has disappeared: *pébrine* is detected in good time. Of late years, in the South of France, horticulture has become a far more important industry than sericulture: early roses and early vegetables are more profitable than mulberry-trees. But the exportation of seed goes on: and that seed is tested by Pasteur's methods.

VI.

ANTHRAX, CHICKEN-CHOLERA, ROUGET

IN 1870, the year of the Franco-German War, Pasteur was forty-eight years old, and had before him twenty-five years of life. The War broke his heart: it is pitiful, to read of his misery. They got him, that September, out of Paris to Arbois. His letters are wild with pain—*Ne faut il pas s'écrier, Heureux les morts!*—and again, *Chacun de mes travaux jusqu'à mon dernier jour portera pour épigraphe, Haine à la Prusse. Vengeance, vengeance.* He was helpless and useless; he had to watch his country tortured, her army defeated, her kingdom divided. Arbois, Geneva, Lyon, Clermont, he was now here, now there, wretched everywhere. The University of Pisa offered him a refuge and a professorship, but he would not leave France; he must console her by his work, he must write her name, in Science, above the name of her enemy. That should be his revenge on Germany, to give himself, body and soul, to the service of France, and to exalt her by his discoveries. To begin with, he might improve

the quality of French beers. He had reformed the making of French wines and vinegars: now, he would set France equal with Germany over the brewing of good beers. At Clermont, early in 1871, he took in hand this great business. For the next five years, to the time of publication, in 1876, of his *Études sur la Bière*, he was at work on brewing.* And, always, he was being led to those later discoveries which were to be the saving not of wines and beers but of legions of human and animal lives. Everything else—crystals and wines and vinegars and silkworms and beers — seems hardly worth talking of, when we recall what he did next for mankind.

* According to Klöcker, this part of Pasteur's work was defective, in that he did not realise the harm done by "wild" yeasts. This defect was remedied by Hansen's later method of yeast-cultures from a single cell. "The relation between Pasteur's and Hansen's work," says Klöcker, "was clearly and forcibly expressed by Delbrück in a lecture delivered in Berlin in 1895: 'Looking back on the last twenty-five years, there are two great epochs marking the scientific development of brewing: Pasteur's work, which was done after 1870, and which is adopted in principle when we nowadays strive, by the setting up of cooling vessels, to ward off external infection, forms one epoch; Hansen's, the other. But Pasteur's attempts could not lead to a fruitful issue, because one link was missing which was furnished by Hansen in his systematic choice of pure yeast. These two men and their discoveries have been the moving forces of the last decade, and have brought brewing to what it is to-day.'"—Klöcker, *On Fermentation Organisms.* Translated by Allan and Millar. Longmans, 1903. Page 15.

The War had found France unfamiliar with Listerism. Thousands and thousands of wounded had died, whom Listerism would have saved. Out of this evil, came the establishment of the antiseptic and aseptic method in Hospital practice in Paris. But those of us who remember the venture of faith in Lister, forty years ago, in this country, can well understand that the way was even harder for Pasteur. The teaching of Lister was concentrated on surgery: kill the "germs of putrefaction" in a wound, and prevent more germs from getting into it, and you will save your patient from wound-infection. The teaching of Pasteur went far beyond the reform of surgery: he was set on the wider doctrine, that specific germs are indeed the causes of specific diseases: he was founding the whole dominion of bacteriology. At once, he came into conflict with the doctors of the old school. In April, 1873, he took his seat as an Associate of the Académie de Médecine: then began the years of controversy over the New Pathology. He had to reckon not with surgeons alone. Some of his opponents had not yet officially recognised the death of the old belief in spontaneous generation: others would not hear of bacteria as the true and only begetters of the infective diseases. He was up against a blank wall of age and convention. Not that he had no following: he

had among his friends Dumas and Claude Bernard; among his disciples, Roux. But his opponents—the men who would not give up their barren way of thinking of diseases, nor admit that it was bound to suffer defeat all along the line—they were hard to bear with, some of them: and it is no wonder, seeing the lives of men, women, and children at stake, that he often lost his temper over the solemn parade of the wrong sort of thoughts.* Take the famous story which Roux tells, one of many instances:—

"In acute abscesses, and in boils, you find a minute round organism, growing in masses: it is easily cultivated in broth. You find it likewise in the infective osteomyelitis of children. Pasteur affirmed that osteomyelitis and boils are two forms of one and the same disease, and that osteomyelitis is a boil in a bone. In 1878, this assertion was much laughed at by surgeons. In cases of infection after childbirth, the blood-clots contain a minute round organism, growing in chains: it looks, especially in pure culture, like a rosary. Pasteur

* "Ce n'était pas qu'avant Pasteur il n'y eût, çà et là, de vives, de soudaines clartés. Mais, loin de se laisser guider par elles, la plupart des médecins continuaient de s'avancer majestueusement au milieu des ténèbres. Dès qu'il était question de maladies meurtrières, de fléaux qui passent sur l'humanité, en avant les grands mots français ou latins, comme le génie épidémique, le *fatum*, le *quid ignotum*, le *quid divinum*. On parlait aussi beaucoup de constitution médicale, mot large, facile, élastique, se prêtant à tout."—*Vie de Pasteur*, ch. viii.

did not hesitate to declare that this micro-organism is the commonest cause of infection among women after delivery. One day, in a discussion, at the Académie de Médecine, on puerperal fever, one of his most popular colleagues was holding forth eloquently on the causes of epidemics in lying-in hospitals. Pasteur, from his seat, interrupted him —*Ce qui cause l'épidémie, ce n'est rien de tout cela: c'est le médecin et son personnel qui transportent le microbe d'une femme malade à une femme saine.* And when the orator answered that he was very much afraid that nobody could ever find that microbe, Pasteur went straight to the blackboard, and drew on it a chain of the micro-organism, saying, *Tenez, voici sa figure.*"—Roux, *L'Œuvre Médicale de Pasteur. Agenda du Chimiste*, 1896, p. 528.

That is how he fought, and beat, the doctors of the old school: and, by that sort of work, he and Lister created what we call modern surgery; and a vast amount of sorrow and sighing fled away, and will never come back, Heaven be praised. It was in 1878, that he drew the *streptococcus* on the blackboard—*There, that's what it's like*—and the words mark the end of the old order. For already, in 1877, he had taken in hand that magnificent series of researches which led up to the protective treatment of sheep and cattle against anthrax.

We in this country have not very much trouble with anthrax (*charbon*). But in France, and elsewhere, forty years ago, it was a frightful scourge of agriculture. There were districts where the

farmers lost, each year, by anthrax alone, 5 per cent. of their cattle and 10 per cent. of their sheep, or more :* the loss to France ran into many millions of francs. The germs of the disease, the *bacillus anthracis*, in the blood, had been seen, under the microscope, so long ago as 1839; but had not been understood. In 1863, Davaine, by the light of Pasteur's work, recognised them for what they are. In 1876, Koch cultivated them outside the body, and reproduced the disease, in mice and rabbits, with this culture: he also noted the presence of spores in the germs, such as Pasteur had noted in the germs of *flacherie*. In 1877, Pasteur set to work. He was opposed, not only by the remnant of the old unbelievers, but by a new array of critics. There was the argument, that anthrax was due not to the germs, but to "something else," some virus which the germs merely accompanied. To refute this argument, he sowed his cultures, from flask to flask, through a series of forty flasks, infecting each flask with one drop from the preceding flask: thus, he diluted the

* "De 1867 à 1870, dans le seul district de Novogorod, en Russie, on enregistra plus de 56,000 cas de mort par l'infection charbonneuse. Chevaux, bœufs, vaches, moutons, tout avait succombé. Atteintes de la contagion sous des formes diverses—il suffit d'une piqûre ou d'une écorchure pour que bergers, bouchers, équarrisseurs, tanneurs s'inoculent la pustule maligne—528 personnes avaient péri."—*Vie de Pasteur*, ch. ix.

imaginary "something else" out of existence: still, the fortieth flask, one drop of it, would produce anthrax in a rabbit or a guinea-pig. There was the argument, that certain rabbits, inoculated with blood from cases of anthrax, had indeed died, but not of anthrax; for the germs of the disease had not been found in their blood. He refuted this argument by showing that the blood, with which they had been inoculated, had contained not only germs of anthrax but germs of septicæmia: the rabbits had died not of anthrax but of septicæmia. There was the notable passage of arms between him and Colin. Were fowls, by nature, proof against anthrax? Pasteur said that they were; Colin, that they were not. In the end, Pasteur solved the question by some experiments as ingenious as they were simple. The normal temperature of fowls is higher than that of mammals. A fowl, if its temperature be brought down, by a cold bath, to that of a rabbit or a guinea-pig, becomes, like them, susceptible to anthrax. Moreover, if a fowl, thus cooled down, be inoculated with anthrax, and then, when the disease begins to show itself, the fowl be taken out of the water and kept warm, the disease will be arrested, and the fowl will recover. These facts, which he demonstrated joyfully, on March 19, 1878, bringing his cage of fowls into the grave presence of the Académie de Médecine, are of

profound significance: and, to the men of his time, they came as a revelation. It is impossible to imagine a set of experiments more absolutely original. On April 30, flinging round to another subject, he spoke on the aseptic method of surgery: that magnificent address, which contains the passage beginning *Si j'avais l'honneur d'être chirurgien.* A touch of irony here: for he was doing more for surgery than any surgeon in all France.

During 1878-80, he gave much time to the study of the natural history of anthrax, travelling through infected districts, and taking the farmers' points of view. It was in the course of this work that he discovered the germs of the disease in earthworms which had fed on buried anthrax-carcases. This discovery enabled him to understand how the infection is conveyed up to the surface-soil and, as it were, haunts this or that field.* It was in 1879 that he proved, by the mere examination of a drop or two of blood, that a patient, supposed to have died of puerperal fever, had died of anthrax: we are accustomed to the routine of bacteriology nowadays, but in 1879 this one case, of itself, was more valuable than a lifetime of "bedside observations." By 1880, he had learned the whole natural history of anthrax; but had not yet found how to protect animals against it.

* Darwin's book, on *The Formation of Vegetable Mould through the Action of Worms*, was published in 1881.

Then, in 1880, came his work on chicken-cholera. For want of room here, many great events of 1880-84 must be left out. His prophetic note in April, 1880, on the bacterial nature of plague; his address at the Académie de Médecine, in October, 1880, on vaccinia and variola; the beginning, in December, 1880, of his work on rabies; his presence at the International Medical Congress in London, in August, 1881: his visit to Bordeaux, next month, in the vain hope of finding yellow fever to be studied there. In 1882, his reception by Renan, on April 27, into the Académie Française; his researches into pleuro-pneumonia of cattle; his controversy with Koch, in September, at the International Congress of Hygiene in Geneva. In 1883, the debate, in the Académie de Médecine, on typhoid fever; the increase of the Government grant to him from 12 to 25 thousand francs; and the despatch of the French cholera expedition to Egypt. In April, 1884, his presence at the Tercentenary Festival of Edinburgh University, and, in August, at the International Medical Congress in Copenhagen. These events are well known to all students of his life. Here, we must keep to the line of his researches on anthrax, chicken-cholera, and rouget.

It was the work on chicken-cholera which led him to the greatest of all his discoveries. See

where he stood, even before 1880. He and his pupils could isolate the germs of this or that disease; could grow them in pure culture, in a test-tube, miles away from a patient; could reproduce the disease, with a drop of this pure culture, in a rabbit or a guinea-pig. We are so familiar, by this time, with stacks of culture-tubes, that we are apt to forget what a miracle it was, and is, to be able thus to bottle a disease. To have, in one's hands, outside the living body, cholera or plague or Malta fever or typhoid or diphtheria—the wonder of it, the sense of seeing, with our own eyes, the real cause, the very stuff, the thing itself, growing in a test-tube—we take it for granted nowadays. Only, from time to time, one more disease is brought within the range of this method, and the wonder is renewed, as we hold in our hands, in a test-tube, syphilis, or epidemic meningitis. Then, in 1880, Pasteur advanced, from the making of cultures, to the attenuation of cultures: and to the supreme discovery, that an attenuated culture is able to confer immunity against a culture at full strength.

A pure culture of the germs of chicken-cholera, he found, lost strength, slowly and steadily, from day to day, by mere keeping. Thus, he could prepare and stock a graduated series of cultures, in every shade of strength, from full virulence to

non-virulence. With one of these attenuated cultures, he could produce in fowls a mild attack of the disease. The fowls, after that, were able to withstand a culture at full virulence. The points of likeness here are plain enough, between Jenner's discovery, how to protect man against small-pox, and Pasteur's discovery, how to protect poultry against the *choléra des poules.** But the points of contrast are not less plain, between the isolated victory over one disease, and the prospect of victory over many diseases.

From the attenuation of one virus, he went on to the attenuation of another: from the *choléra des poules* to anthrax. After many difficulties, he was successful. In May, 1881, came the final demonstration of his method, near Melun, on the farm at Pouilly-le-fort. The story has been told a thousand times, and will bear telling to the end of time. He took fifty sheep, in two lots of five and twenty each:

* It was inevitable, that the words *vaccine* and *vaccination* should be applied to this method of protective treatment, even though *vacca* the cow had nothing to do with it. Pasteur himself, in his address to the International Medical Congress in London, August 8, 1881, said, "J'ai donné à l'expression de vaccination une extension que la science, je l'espère, consacrera comme un hommage au mérite et aux immenses services rendus par un des plus grands hommes de l'Angleterre, votre Jenner. Quel bonheur pour moi de glorifier ce nom immortel sur le sol même de la noble et hospitalière cité de Londres."—*Trans. Int. Med. Congress*, 1881, vol. i., p. 90.

he left the one lot to Nature: he protected the other lot with attenuated virus. Then, on May 31, he inoculated all fifty sheep with a very strong culture. Two days later, a great crowd assembled at Pouilly-le-fort: men of science, farmers, delegates from agricultural societies, journalists. Of the 25 sheep left to Nature, 22 were dead, 2 were dying, 1 was sickening. Of the 25 protected sheep, all were in good health.

That was more than thirty years ago. From that time to this, the protective treatment of sheep and cattle against anthrax has been in use. It had its critics—Koch, 32 years ago, and Müller, I know not when, and the Hungarian Government, 30 years ago—but we need not mind what was said 30 years ago. *Securus judicat orbis terrarum.* The practical men, the agriculturists and the breeders of stock, are well aware that the treatment does protect their sheep and cattle.* Nor is this the only benefit

* Dr. Besredka, of the Pasteur Institute in Paris, told me, a few years ago, that the number of doses of this vaccine sent out from the Institute was larger every year. Two doses are allowed for each animal. In 1908, the number of doses sent out was 2,600,000. An article this year in the *Revue des Deux Mondes* (February, 1914) says that more than 40 million doses have by this time been sent out. See also Sir Stewart Stockman's evidence before the Royal Commission on Vivisection, December 5, 1906: "It may not always be worth one's while to inoculate. That is to say, on a farm where a few cases occur every year, you would not inoculate: and the best method in such a case would be, as he (Professor Müller) says, to destroy the

which has come of Pasteur's researches on anthrax. For we have also Sclavo's serum-treatment of anthrax in man: and the value of this treatment is not open to doubt. See, on this point, the Reports of the Bradford Anthrax Investigation Board, 1910-12. The authority of this Board, to whom Dr. Eurich is bacteriologist, may truly be called final.

In France—to say nothing of other countries—between 1882 and 1893, more than three million sheep, and more than 400,000 cattle, received the protective treatment. In March, 1894, in the *Annales de l'Institut Pasteur*, Chamberland published the results:

"After the famous experiments at Pouilly-le-fort, MM. Pasteur and Roux entrusted to me all the method and practice of vaccinations against anthrax. Twelve years have passed, and it is time now to put together the results and form a final estimate of the value of these preventive inoculations.

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carcases, and all sources of the infection, and prevent infection being brought in. But then there are countries where you cannot do that, and there are places which are already so badly infected that, even if you do destroy the carcases, the disease will go on, since the soil is badly contaminated. . . . Statistics collected in Hungary on over 11½ millions of inoculated animals show that the results have been practically the same as in France. They talk of farms where the loss which was 10 per cent. has been reduced to under 1 per cent." We in this country have not *champs maudits*, *montagnes maudites*, *fermes à charbon*, such as they had 40 years ago in France.

". . . A certain number of veterinary surgeons neglect to send their reports at the end of the year. Indeed, the reports which come to us tend to be fewer every year. The fact is, that many veterinary surgeons who make inoculations every year content themselves with writing, 'The results are always very good; it is useless to send you reports which are always the same thing.'

". . . In the twelve years up to January 1 of this year (1894) we have had exact returns as to 1,788,879 sheep and 200,962 cattle—about half of all those that were vaccinated. . . . The total loss of sheep is about 1 per cent.: the average for the twelve years is 0·94. So we may say that the whole average loss of vaccinated sheep, whether from vaccination or from the disease itself, is about 1 per cent. The loss of vaccinated cattle is even less. For the period of twelve years, it is 0·34, or about one-third per cent.

" These results are extremely satisfactory. It is important to note that the average animal death-rate from *charbon*, in the days before vaccination—the average given in these reports—is estimated at 10 per cent. among sheep, and 5 per cent. among cattle. But, even if we put it at 6 per cent. for sheep, and 3½ per cent. for cattle, and say that the worth of a sheep is 30 francs, and of an ox or a cow 150 francs—which is well below their real value—even then it is obvious that the advantage of these vaccinations to French agriculture is about five million francs in sheep, and two million in cattle. And these figures are rather too low than too high."

It would be easy to collect a multitude of instances. Here is one: in letters, this year, from

Mr. Livingstone-Learmouth, of Guildford. "As manager of a very large estancia in the Argentine, I had to superintend the vaccination of some 200,000 injections of vaccine against anthrax. I had seen thousands of cattle and sheep die of this plague. Thanks to Pasteur and research we saved the lives of the rest. . . . I spent about 20 years there. There were areas, almost 'zones,' where the land was so impregnated with anthrax, that cattle-breeding ceased, until inoculation by the Pasteur treatment enabled men to resume cattle-breeding." He goes on to speak of the value of the serum-treatment, in cases of infection of man. "The gauchos could not be brought to understand the danger of infection, and would insist on skinning animals which had died of this disease, always with the idea of using the hide for their private use. When the Pasteur Institute gave us the antitoxin, we were able to save many lives. . . . I went out to South Africa, in 1909, and selected the cattle estates for ———, some 1,250,000 acres. Had Pasteur not initiated his protective system, I would not have taken up one acre. But I found in Rhodesia a well-established laboratory, which owes its existence to scientific research, and without hesitation I took up that land which had been devastated by disease, and was then practically unoccupied by men or cattle. Thanks to

scientific research, men and cattle can now live there."

From anthrax, Pasteur went on to the study of swine-erysipelas, *rouget, mal rouge.* Thuillier, in March, 1882, had discovered the germs of this disease: and, in November of that year, Pasteur and he began to work out a method of protective treatment. But the rush of graver affairs in Paris, and the death of Thuillier—he went on the cholera-expedition to Egypt, and died of cholera, in Alexandria—delayed the study of *rouget.* Still, by 1886, the work was done. Chamberland in 1894 reported as follows:

"Some years after the discovery of vaccination against *charbon*, M. Pasteur discovered the vaccine for a disease of swine known under the name of *rouget.* From 1886, these vaccines were sent out under the same conditions as the vaccines against *charbon.* . . . The total average of losses during the past seven years is 1·45 per cent., or about 1½ per cent. This average is appreciably higher than the average for *charbon.* But it must be noted that the mortality from *rouget* among swine, before vaccination, was much higher than that from *charbon* among sheep. It was about 20 per cent.; a certain number of reports speak of losses of 60 and even 80 per cent.: so that almost all the veterinary surgeons are loud in their praises of the new vaccination."

More than 10 million doses of this vaccine have been sent out from the Institute. (See the *Revue*

des Deux Mondes, February, 1914.) At the present time, use is made of a vaccine-treatment combined with a serum-treatment. This combined method was worked out by Leclainche, and gives better results than the treatment by vaccine alone. Leclainche's method is described, and commended, in leaflet 227 of the Board of Agriculture and Fisheries, December, 1909.

VII.

RABIES

It was in December, 1880, that Pasteur took in hand the study of rabies. It was on July 6, 1885, that he first used on man the protective treatment which he had proved on animals. In a few months, we shall come to the thirtieth anniversary of that event: there ought to be a calendar of the healing art, to remind us of all such days.

He had discovered, in 1880, how to attenuate the virus of the fowl-cholera. He had discovered, in 1881, how to intensify the virus of anthrax, by inoculating with an attenuated virus a series of newly-born guinea-pigs. The attenuated virus, not strong enough to kill a guinea-pig which was several days old, was strong enough to kill a guinea-pig which was one day old. By passing it through a series of one-day-old guinea-pigs, inoculating each of them with the blood of its predecessor in the series, he was able to intensify it, till it was strong enough to kill full-grown guinea-pigs, and even to kill sheep.

By this twofold power, not only to bring down a virus, point by point, from full virulence to non-virulence, but also to exalt a virus, point by point, from non-virulence to full virulence, he was able to obtain his *virus fixe*, his standard virus. He was able to have, in his hands, a virus of known strength. He was able to measure out an exact dose of this virus, calculated to produce a known effect on an animal of known weight. And, as with fowl-cholera and anthrax, so with rabies, he was able to confer immunity, with a graduated series of attenuations of the virus, against the disease itself. That is to say, he could begin with a dose of complete non-virulence: next day, a dose of minimum virulence: next day, a dose one shade stronger: and so on. By this method, he could advance, till the patient was immunised against the disease itself. The patient, guarded each day by the dose of the previous day, would be able, on the last day of the treatment, to take without harm a dose as strong as anything that the disease itself could do to him. The treatment would be carried out during the time when the disease itself was latent in the scar of the bite, locked up, asleep, inert. Some day, it might be wanting to flare up. On that day, it would find itself outwitted: the patient—so to speak—would have had it already, by instalments: he would have immunised himself,

through and through, by a leisurely, accurately measured, standardised course of progressive doses: and the latent virus would thus have lost its one and only opportunity of killing him.

The working out of this theory, from 1881 to 1885, was beset with all kinds of difficulties. To guide him, he had the conviction that rabies does not "come of itself": that dogs cannot "go mad": that rabies must be begotten of rabies. But this fact, which now we all accept, was held open to doubt, thirty or more years ago. Again, he was unable to discover the germs of the disease: he had therefore to alter his methods of research. It goes without saying, that the work was not only difficult but dangerous: he did not mind that: but he did mind, heavily, the final step, from the immunising of animals to the immunising of man. He was sixty-three, when he took that step: and it is certain that the frightful strain of 1885 aged him. Happily for mankind, his work, by 1885, was everlasting: he had founded and established a new kingdom of science: he had taught the whole world a new way of thinking of the infective diseases, and a new way of dealing with them.

His experimental study of rabies began, of course, with inoculations of saliva. So early as

December, 1880, he was experimenting with the saliva of a child who had died in one of the Paris hospitals of hydrophobia. He was experimenting, also, with the saliva of rabid animals: he would be off, at a moment's notice, to see a captive mad dog, and would make his inoculations then and there. Roux has told us of one of these experiments: "The animal was a huge bull-dog, foaming at the mouth and howling in its cage. All attempts to get it to bite and thus infect a rabbit had failed. 'But we *must* inoculate the rabbits with the saliva,' said Pasteur. A noose was made and thrown, the dog was caught and dragged to the bars of the cage, and its jaws were tied half-open. It was then held down on a table, while Pasteur, with a fine glass tube between his lips, leaned over the dog, and drew into the tube a few drops of the saliva."

But these experiments with saliva were not of much help to him. In the saliva of rabies, and of many other diseases, and even in healthy mouths, all sorts of germs are present—*'tis an unweeded garden*—and, though his rabbits died after inoculation with saliva, he could not prove, in every case, that they had died of rabies. Besides, with the inoculation of saliva, the latent period of the disease was quite indefinite: it might be some

weeks before the disease flared up in the rabbit, or it might be some months: or the disease might wholly fail to flare up. Neither inoculation with saliva, nor inoculation with blood, led him to any discovery. Then, came the next stage of his work. He adopted the theory, that rabies must be studied, not in the saliva or the blood, but in the brain and the spinal cord: that the disease must be regarded as a poison taking up its chief abode in the brain and the cord, especially in that citadel of life, the *medulla oblongata*, the "bulb," the part of the cord which is nearest to the brain. By a strictly aseptic method of experimenting, he succeeded, where Galtier had failed, in producing the disease, in dogs and rabbits, by putting under the skin a measured quantity of the medulla of a dog dead of the disease. This method, he found was surer to give a positive result than the use of saliva. Still, he had to meet two difficulties; he had to shorten up the latent period, and he had to make certain of obtaining a positive result in every case without exception. Then came the turning-point of his work. He put the dose of medulla not under the skin, but on the surface of the brain, under the *dura mater*, the membrane which encloses the brain: that is to say, he put the disease where it was most sure of rapid development. The animals were chloroformed; a little disc of bone was removed

with a trephine; the dose of medulla, rubbed up in a few drops of sterilised fluid, was put under the dura mater through a hollow needle; and the wound was closed. This subdural method was infallible: it gave a positive result in every case, and a more rapid development of the disease. The latent period, with this method, was never more than twenty days.

But it was not enough, that he should shorten the latent period: he must fix it, he must get it down to a standard number of days, and maintain it there. He could do nothing, till he had done that. He must have his *virus fixe:* he must be able to determine the very day on which the disease should flare up. And this he did. As he had intensified the virus of anthrax, by passing it through a series of new-born guinea-pigs, so he now intensified the virus of rabies, by passing it through a series of rabbits: the latent period, as the series of inoculations went on, became shorter and shorter. Finally, it came down to seven days, or a few hours less. There, it stopped: it could not be shortened below six to seven days. The virus now had attained its fullest strength, and was even stronger than the virus of an ordinary case of the disease. Moreover, it retained its strength, unimpaired, through any number of subsequent passages from animal to animal. It would

always have a latent period of six to seven days; and it would always cause death.*

Then came the first step toward a protective treatment. As he had attenuated the virus of fowl-cholera, by mere keeping, so he now attenuated the virus of rabies, by mere keeping. If the spinal cord of a rabbit, which had died of an inoculation of *virus fixe*, were removed—of course by a strictly aseptic method—and kept in an aseptic flask, in dried and filtered air, in the dark, at a constant temperature, it would steadily lose virulence, day by day. At the end of fourteen days, it would be wholly non-virulent. Thus, by inoculating a sufficient number of rabbits, he was able to prepare and stock, in a complete set of cords, the dried virus of rabies, in every shade of strength, from non-virulence up to fullest virulence. With measured doses of these cords, rubbed up in a little water, and injected under the skin, he could immunise dogs; beginning with a dose of fourteen-days' cord, then a dose of thirteen-days' cord, and so on, up to a dose of cord at full virulence. These dogs, thus immunised, were submitted to the bite of mad dogs, or even to subdural inoculation; and took no harm.

That is the story, in four pages, of near four years of work. In May, 1884, he asked the French

* It is satisfactory to know that rabbits affected with rabies do not suffer in the same way as dogs and some other animals, but become subject to a painless kind of paralysis.

Government to appoint a Commission to report on his method. In August, having witnessed many experiments, the Commission reported favourably of "these magnificent results, which are so highly honourable to French science and confer on him a new title to the gratitude of humanity": and the Government assigned to him a piece of land at Villeneuve, for the purposes of his work. There was much still to be done: the Commission must verify every point, with further experiments and control-experiments. By September, 1884, he had attained the last step of his method: he had proved that he could prevent the disease in dogs already bitten:

"I have not yet dared to attempt anything on man, in spite of my confidence in the result, and in spite of the many occasions which have come to me since my last address at the Académie des Sciences. I am too much afraid of some reverse which would compromise the future: I must first wait till I have got a whole crowd of successful results on animals. As for these results—things are going well. I have already several cases of dogs immunised after rabic bites. I take two dogs: I have them bitten by a mad dog. I vaccinate the one, and I leave the other without treatment. The latter dies of rabies: the former withstands it. But, however I should multiply my cases of protection of dogs, I think that my hand will shake when I have to go on to man." *

* He writes this, on September 22, 1884, to the Emperor of Brazil, who was keenly interested in his work. And he

By May, 1885, more than 100 dogs, beside other animals, were under observation, at Villeneuve or elsewhere. Experiments, control-experiments, dogs immunised before infection, dogs immunised after infection—the whole method proved again and again, we might say now, proved so plainly that more experimenting would be worse than useless—then, on Monday morning, July 6, 1885, an Alsatian woman brought her child, Joseph Meister, to the Rue d'Ulm. He had been attacked, two days before, by a dog, thrown down, bitten in fourteen places, worst on the hands, and found covered with the dog's saliva and his own blood. The dog had then attacked its own master, and been shot: and its body had shown evidence of rabies. The child's wounds had not been carbolised until twelve hours after they had been inflicted. He had been sent to Pasteur by Dr. Weber, of Villé. He could hardly walk for pain: he was nine years old. Pasteur immediately took a room in Paris for him and his mother: that evening, he and

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goes on to suggest that criminals, condemned to death, should be allowed to choose, on the eve of their execution, between being hanged and being experimented on, for the discovery of a preventive or curative treatment of rabies or cholera. The proposal is open to criticism: but none of us, surely, if he knew for certain that he must be hanged to-morrow, would refuse to-day this good prospect of life, unless he were sincerely desirous of death.

Vulpian and Grancher saw the child, and consulted over him: and, in view of the severity, the number, and the position of the wounds—for bites on the hands are of a high degree of danger—they decided that they dared not refuse to treat him. The story of Pasteur's loving anxiety and sleepless nights over the child—who is, or lately was, in the service of the Pasteur Institute—must be read, every word of it, in the *Vie de Pasteur*. In October, came his second patient, the young shepherd, Jupille, who to protect some little boys had collared and killed a mad dog, and got frightfully bitten: he was sent by the Mayor of Villers-Farlay: six days had passed before he arrived in Paris. He, likewise, is in the service of the Institute.

The news of these two cases brought a rush of patients to the Rue d'Ulm: and a formal "Service de la Rage" was organised. By March 1, 1886, the number of patients treated was 350: of whom only one had died, a little girl, Louise Pelletier, badly bitten on the head, and not brought for treatment until 37 days afterwards. Then came the tragedy of the arrival of 19 Russian patients from Smolensk, who had been bitten, and some of them badly mauled, by a mad wolf. It was fifteen days before they arrived: and the bite of a mad wolf is even worse than that of a mad dog. Of these 19 Russians, 3 died. The total number of patients

treated, in 1886, was 2,671 : of whom 25 died =0·94 per cent.

It is to be noted, that the full advantage of the treatment is gained not immediately, on the last day of the treatment, but a fortnight later. That is to say, if the last dose of protective cord were given on the last day of a month, the patient would not attain the highest degree of immunity until the middle of the next month. This belief is supported not only by experiments on animals, but by observations on man. Therefore, at the Pasteur Institutes, if the disease flares up within 15 days after the last day of treatment, the case is reckoned as one of those cases where the treatment was begun too late: and is not included in the general table of results, but is mentioned separately. The number of these incompleted cases is not enough to touch the fact that Pasteur's method brought down the death-rate, in 1886, to 1 per cent., and has kept it, from then to now, at 1 per cent., or less than 1 per cent. Bernstein, with great industry, has compiled the results obtained by 40 Anti-rabic Institutes over a period of 18 years. The total number of persons treated was 104,347. Of these, 560 died, 14 or more days after treatment = 0·54 per cent. If we add the cases which died during the first fortnight after treatment, the mortality, still, is only 0·73 per cent. (Remlinger, *Bibliothèque de*

Thérapeutique, vol. xii., p. 116. Paris, Baillière Fils, 1912.) Later statistics, compiled by Remlinger, give a percentage which is even lower.

The patients are divided into three classes. In class A, the animals which bit them are proved to have been rabid, by the development of rabies in other animals either bitten by them or inoculated with their medulla. In class B, the animals are judged to have been rabid, by examination of their bodies after death. In class C, the animals are only suspected to have been rabid. But, even in class A, the mortality is less than 1 per cent.

The most careful estimate of the mortality among persons who have been bitten by dogs judged to be rabid, but have not been treated by Pasteur's method, is 16 per cent.

It is not impossible, in theory, that a patient, after returning home, should die, and his death not be reported to the Institute where he was treated: but such an event, if it has ever happened, must be very rare. Certainly, it would not alter the fact, that the world's record has been kept down, from 1886 to 1914, at less than 1 per cent.

Pasteur's original method is still observed at the Paris Institute. The formula varies, of course, according to the number, situation, and gravity of the bites: but the method is one and the same. We may take, for instance, the formula for

cases of a severe type, but not the severest type: multiple bites on the hand, but none on the head:

EIGHTEEN DAYS' TREATMENT.

Day of Treatment.	Number of Days of Drying of Cord.
1st day	14–13 days.
2nd ,, ...	12–11 ,,
3rd ,, ...	10–9 ,,
4th ,, ...	8–7 ,,
5th ,, ...	6 ,,
6th ,, ...	5 ,,
7th ,, ...	5 ,,
8th ,, ...	4 ,,
9th ,, ...	3 ,,
10th ,, ...	5 ,,
11th ,, ...	5 ,,
12th ,, ...	4 ,,
13th ,, ...	4 ,,
14th ,, ...	3 ,,
15th ,, ...	3 ,,
16th ,, ...	3 ,,
17th ,, ...	4 ,,
18th ,, ...	3 ,,

The Paris figures, for the first ten years, are as follows:

Year.	Patients.	Deaths.	Mortality Per Cent.
1886	2,671	25	0·94
1887	1,770	14	0·97
1888	1,622	9	0·55
1889	1,830	7	0·38
1890	1,540	5	0·32
1891	1,559	4	0·25
1892	1,790	4	0·22
1893	1,648	6	0·36
1894	1,387	7	0·50
1895	1,520	5	0·33

Or take the figures from the Pasteur Institute at Tunis. This Institute has had, altogether, 4,568 complete cases, with only 16 deaths=0·35 per cent. In 1912, it had 367 completed cases, with 2 deaths. (*Archives de l'Institut Pasteur de Tunis*, 1913, p. 136.)

Of late years, the establishment of Anti-rabic Institutes far and wide has greatly reduced the number of patients at the Paris Institute. The recent figures from the Paris Institute are as follows: In 1910, 401 cases, 0 death: in 1911, 343 cases, 1 death: in 1912, 395 cases, 0 death. The number of cases in class A, in these three years, was 147.

In England, in 1886, the Government appointed a Committee to inquire into Pasteur's method. It reported favourably: and, after a Mansion House Meeting on July 1, 1889, Sir James Whitehead presiding, a thank-offering of 40,000 francs was sent to the Pasteur Institute. We have to note, that the passing of the Muzzling Act, and the consequent stamping out of rabies in this island, were largely due to Pasteur's influence.* But what Act could

* "The freedom of England from rabies I take to be one of the great achievements of modern science: and we owe it entirely to M. Pasteur. . . . I had the honour of acting as secretary of a Committee that was appointed by the Government to inquire into M. Pasteur's treatment; and, when the Committee was in Paris, M. Pasteur said to us, 'Why do you come here to study my method? . . . You do not require it in England at all. I have proved that this is an

muzzle all the pariah-dogs of India, and all the wolves in Russia?

It is not claimed, that among so many tens of thousands of cases treated, in all parts of the world, there has never been a disaster. But it is absolutely certain, that the method has indeed brought down the mortality almost to vanishing point. The estimate of 16 per cent. must include many cases where the biting animal was not really mad. Take, therefore, 1,000 cases, all of them belonging to class A. It is safe to say that the mortality among them, without Pasteur's treatment, would be far more than 16 per cent. With Pasteur's treatment, it is less than 1 per cent.

But this final work told on him: it made him older than his years. In November, 1888, the Pasteur Institute was opened: it was the gift not of France alone, but of many countries, to Pasteur: "but he was a broken and tired old man, and it was sad to see how his hard work and the opposition he had so often encountered had aged him."*

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infectious disease: all you have to do is to establish a brief quarantine covering the incubation period, muzzle all your dogs at the present moment, and in a few years you will be free.' When the Committee returned and reported to the Houses of Parliament, this point, of course, was always before us."—*Sir Victor Horsley, Evidence before the Royal Commission on Vivisection, November* 13, 1907.

* From Dr. Sandwith's admirable Gresham Lecture, *Pasteur, Science and Medicine*, in the *Practitioner*, December, 1909. Published, also, by the Research Defence Society.

Paris, le 10 mai 1889

Cher et vénéré Maître

J'allais prendre la plume pour vous écrire lorsque j'ai reçu votre affectueuse lettre

J'ai le vif regret de vous dire que malgré mon désir exprimé à maintes reprises, de me rendre à Londres avec le Docteur Roux et profiter de votre très gracieuse hospitalité. mon entourage et Mme Pasteur, la première, s'oppose absolument à mon voyage. Comment ne pas obéir! Excusez-moi donc cher maître. Sir Roscoe qui m'a fait le grand plaisir de venir me voir, il y a peu de jours, à son retour de Nice, pourra vous dire combien, en effet, je suis peu présentable. Lui-même a approuvé la prudence de ma femme et de mes enfants

Je fais des vœux bien empressés pour que ces quelques lignes trouvent Mme Paget en meilleur état de santé. Ma famille se joint à moi pour offrir à Mme Paget nos souhaits de prompt rétablissement.

Veuillez agréer, cher et vénéré maître, pour vous et Mlle Paget l'expression de mes sentiments les plus reconnaissants et dévoués

L Pasteur

FACSIMILE OF A LETTER FROM PASTEUR TO SIR JAMES PAGET

Still, he guided the work of the younger men, the *Pastorians*, the workers at the Institute: he was incessantly helping and encouraging them. The story of his old age must be read in the *Vie de Pasteur*. On June 13, 1895, he said goodbye to the Institute. He died at Villeneuve, on September 28 of that year. Madame Pasteur died at Arbois, September 24, 1910.

Permission has been given by the editor of the *Spectator* to quote from an article, by an anonymous writer, which was published in that journal in 1910:—

"There are more than sixty Pasteur Institutes: but I am thinking of the Paris Institute. At the end of one of its long corridors, down a few steps, is the little chapel where Pasteur lies. . . . From the work of the place, done in the spirit of the Master, and to his honour, you go straight to him. Where he worked, there he rests.

"Walls, pavement, and low-vaulted roof, this little chapel, every inch of it, is beautiful: to see its equal you must visit Rome or Ravenna. On its walls of rare marbles are the names of his great discoveries—Dyssymétrie Moléculaire, Fermentations, Générations dites Spontanées, Etudes sur le Vin, Maladies des Vers à Soie, Etudes sur la Bière, Maladies Virulentes, Virus Vaccins, Prophylaxie de la Rage. In the mosaics, of gold and of all colours, you read them again; in the wreathed pattern of hops, vines, and mulberry leaves, and in the figures of cattle, sheep, dogs, and poultry. . In

the vault over his grave are four great white angels, Faith, Hope, Charity, and Science. From time to time Mass is said in the chapel: the altar is of white marble. Twice a year, on the day of the Master's birth and the day of his death, the workers at the Institute, the "Pastorians," come to the chapel, some of them bringing flowers in memory of him, and afterwards pay a visit of ceremony to Madame Pasteur, whose apartments are on the second floor of the Institute, above the chapel. . . .

"Yet, to me, who remember him, saw him, heard him talk, shook hands with him, all the adornments round his grave were not sufficient, and the half was not told me. For he was, it seems to me, the most perfect man who has ever entered the kingdom of Science. His devotion to home, his gentleness, humility, faith, patriotism, honour, shine like stars. And if I take, so far as I can, which is not far, his scientific life alone, apart from his spiritual life, I recognise in it also the same clear evidence of inspiration. For he is drawn or led forward, as it were according to a carefully devised scheme, from each discovery to the next. First, mathematics: the pupil-teacher's board and lodging and twelve pounds a year at the College of Besançon. Then chemistry, and the run of the great Ecole Normale, where he could think and make experiments and learn without ceasing: and here the voices begin to call him, as they called to Joan of Arc, to help France; and not France only did he help. Then he is advanced, from the study of crystalline forms, to the study of ferments. . . .

"Out of it all, out of his magnificent studies of fowl-cholera, anthrax, osteo-myelitis, and

puerperal fever, came this power, not dreamed of before him, the power to standardise this or that disease: to have its germs growing in a test-tube, and to have them of a definite strength: to graduate them, in a regular series, from non-virulence to full virulence: to stock a disease in all shades of strength: and to use these bottled poisons, in their proper order, to immunise men or animals against the natural disease. Thus, at last, when he had re-created pathology, and had accomplished more for doctors than whole ages of their work could accomplish, he was led to his last appointed discovery, the preventive treatment against rabies.

"That was in 1885: and, about 1890, he began to grow old. He had worked so hard, and had made his way, with infinite patience, against so much opposition, some of it intelligent enough, some of it foolish past all telling. Henceforth, he must begin to let his work pass into the hands of younger men. Let it pass? Why, it had passed, already, into the hands of all men. It was become part of the doctor's daily practice, part of the routine of every hospital, part of the method of the medical sciences, part of all nursing, part of all housekeeping, part of all farming, part of all brewing. There is no country on earth which is not the richer and the happier because of him.

"Then came enfeeblement, and a year of quiet resignation; and, in September, 1895, his death. It is recorded of him that he died holding the crucifix in one hand, and in the other his wife's hand. Here was a life, within the limits of humanity, wellnigh perfect. He worked incessantly: he went through poverty, bereavement,

ill-health, opposition: he lived to see his doctrines current over all the world, his facts enthroned, his methods applied to a thousand affairs of manufacture and agriculture, his science put in practice by all doctors and surgeons, his name praised and blessed by mankind: and the very animals, if they could speak, would say the same. Genius: that is the only word. When genius does come to earth, which is not so often as some clever people think, it chooses now and again strange tabernacles: but here was a man whose spiritual life was no less admirable than his scientific life. In brief, nothing is too good to say of him: and the decorations of his grave, once you know his work, are poor, when you think what he was and what he did. Still, it is well that he should lie close to the work of the Institute, close to the heart of Paris, with Faith, Hope, Love, and Science watching over him."

THE PASTEUR CHAPEL

VIII.

TUBERCULOSIS

LAENNEC (1791–1826), the inventor of the stethoscope, may also be called the founder of our present knowledge of tuberculosis as a separate disease of itself. Before his time, it had mostly been regarded as a "degeneration"; though its infective nature had not gone without some recognition.

Klencke, in 1843, showed that it was communicable to animals by inoculation. Villemin, in 1865–68, showed its transmissibility from animal to animal, and the identity of phthisis (tuberculosis of the lungs) with those tuberculous affections of the skin and of the joints which used to be called scrofulous.* Chauveau, in 1868, showed that the

* "Villemin, by carefully conceived and conducted experiments on animals, showed that tuberculosis was an infective disease, due to a specific virus of a parasitic nature, which was introduced from without. He showed that the virus was capable of multiplying indefinitely in the bodies of animals, and of being handed on from one animal to another by inoculation. He also demonstrated by experiments on animals the causal unity of the numerous manifestations of

disease could be induced in animals not only by inoculation, but by mixing tuberculous matter with their food. Cohnheim, in 1880, laid down the law of all research into the nature of the disease :—

"Everything is tuberculous, that can produce tuberculous disease by inoculation in animals which are susceptible to that disease: and nothing, which cannot do this, is tuberculous."

In 1881, at the International Medical Congress in London, Koch showed to some members of the Congress the tubercle bacillus, the actual germs of the disease. His first published account of this great discovery is dated March 24, 1882. There are two sentences in it which deserve the attention of all men :—

"Henceforth, in our warfare against this fearful scourge of our race, we have to reckon not with a nameless something, but with a definite inmate of the body; its conditions of existence are for the most part already known, and can be further studied. . . . Before all things, we must shut off the sources whence the infective material comes; so far as it lies in the power of man to do this." *

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tuberculosis, such as phthisis, caseous pneumonia, scrofula, lupus, and joint disease, etc.; and also the important fact that 'grapes,' a common disease of cattle, was due to the same virus."—Evidence of Dr. C. J. Martin, Director of the Lister Institute, before the Royal Commission on Vivisection, July 10, 1907.

* "In Zukunft wird man es im Kampf gegen diese schreckliche Plage des Menschengeschlechter nicht mehr mit

Beside Koch's work on tuberculosis, there is the whole range of his work on anthrax, wound-infection, cholera, typhoid, rinderpest, malaria, and sleeping sickness. Moreover, he greatly extended the use of solid culture-media, such as gelatin; and the use of differential stains.* These two methods are the very making of bacteriology.

It is true that he was not infallible: but he rendered memorable services to the world. He discovered and proved the association of tuberculosis with *a definite inmate of the body:* it is the very phrase of Pasteur, *Tenez, voici sa figure.* He led everybody to seek methods of *shutting off the sources of infection:* it is the very method of Pasteur and Lister, the antiseptic and aseptic method. The national crusades against tuberculosis, every inch of the way, are guided by the knowledge that the tubercular diseases are of the nature of infective diseases. It would be absurd, here, to pretend to give an account of the past thirty years of work on tuberculosis. But none

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einem unbestimmten Etwas, sondern mit einem fassbaren Parasiten zu thun haben, dessen Lebensbedingungen zum grössten Theil bekannt sind und noch weiter erforscht werden. . . . Es müssen vor allen Dingen die Quellen, aus denen der Infections-stoff fliesst, so weit es in menschlichen Macht liegt, verschlossen werden."

* See his *Investigations into the Etiology of Traumatic Infective Diseases.* Translated by W. Watson Cheyne. London: The New Sydenham Society: 1880.

can fail to understand the profound influence, on that work, of Koch's discovery.

1. He made it possible to detect the disease by microscopic examination of the sputa, or of matter from an abscess. This test is in daily practice all over the world.

2. The present methods of vaccine-therapy in the tubercular diseases all go back to his use, in 1890, of tuberculin. That first use was dangerous: it did good in some cases; but in some cases it was disastrous. It is close on a quarter of a century since 1890. During this long time, many new forms of tuberculin have been devised; the indications for its use have been studied with the utmost carefulness; and it is now in general use, for a large proportion of cases, with good results.

3. The tuberculin-test for cattle has been adopted everywhere, and has been a very great advantage to agriculture. The Royal Commission on Tuberculosis, in 1913, issued a supplementary report, by Dr. Cobbett and Dr. Stanley Griffith, on this test: making the fact plain, that with cattle, swine, goats, and horses, it is of the utmost value. Among 250 tuberculous cattle, no less than 88·8 per cent. reacted to the test: among 1,217 normal cattle, only 0·4 per cent. gave a reaction. Of

10 tuberculous horses, all reacted: of 23 normal horses, none. Among swine and goats, the results were no less decisive.

4. In our great cities, the milk-supply is regularly tested, lest it should convey the germs of tubercle. In London, for instance, samples of milk are sent, by order of the London County Council, to the Lister Institute. The milk is put on a centrifugal machine; and a few drops of the sediment are put under the skin of a guinea-pig. If the guinea-pig shows signs of tubercle, it is killed and examined, and the infection is traced back to its source.

5. It has been proved that the sputa, dried and blown about in dust, are capable of conveying infection. The general recognition of this fact has led to the enforcement of rules against spitting in public places, and to the adoption of other sanitary measures to prevent the spread of the disease. Especially, it has been made compulsorily notifiable: not only consumption, but surgical tuberculosis, must be notified: so that all necessary disinfection of premises, and protection of small children against infection, may be taken in hand. Forty years ago, any proposal for the compulsory notification of phthisis would have been met with a storm of ridicule.

6. The old belief, that consumption was innate and inevitable, has given way to the more hopeful assurance that the actual germs of the disease are not transmitted.

In all these ways, Koch's discovery told, and is telling, on the course of the world. Those of us who are old can remember the time when consumption was regarded as a sort of congenital affliction, wellnigh hopeless, non-infective, non-communicable from animals to man, non-discoverable (save in a very advanced stage) by any microscope-test. It was fought, by doctors and nurses, in hospital and in private practice, to the best of their power: but there was no talk of the whole nation fighting it. And we may fairly say of Koch, that he, when he proved that the disease is due "not to a nameless something, but to a definite inmate of the body," set every civilised country thinking what could be done, by national united effort, to "shut off the sources whence the infective material comes."

IX.

DIPHTHERIA

It is just twenty years since Roux, in September, 1894, at the Congress of Hygiene and Demography in Buda-Pesth, spread the good news of the discovery of diphtheria-antitoxin. It was in September, 1895, that Pasteur, dying at Villeneuve, had round him the whole scene of the making of the antitoxin: every day, it was saving children from death.

Klebs, in 1875, had discovered the germs of the disease: and Loeffler, in 1882, obtained them in pure culture. They are therefore called the Klebs-Loeffler bacillus. Roux and Yersin, in 1888-90, proved that the toxin, the product of the germs, could be separated, by filtration, from the germs: and this toxin, though it contained no germs, would none the less produce, in animals, the effects of the disease itself. By December, 1890, Behring and Kitasato were able, with graduated doses of this toxin, to immunise animals against diphtheria:

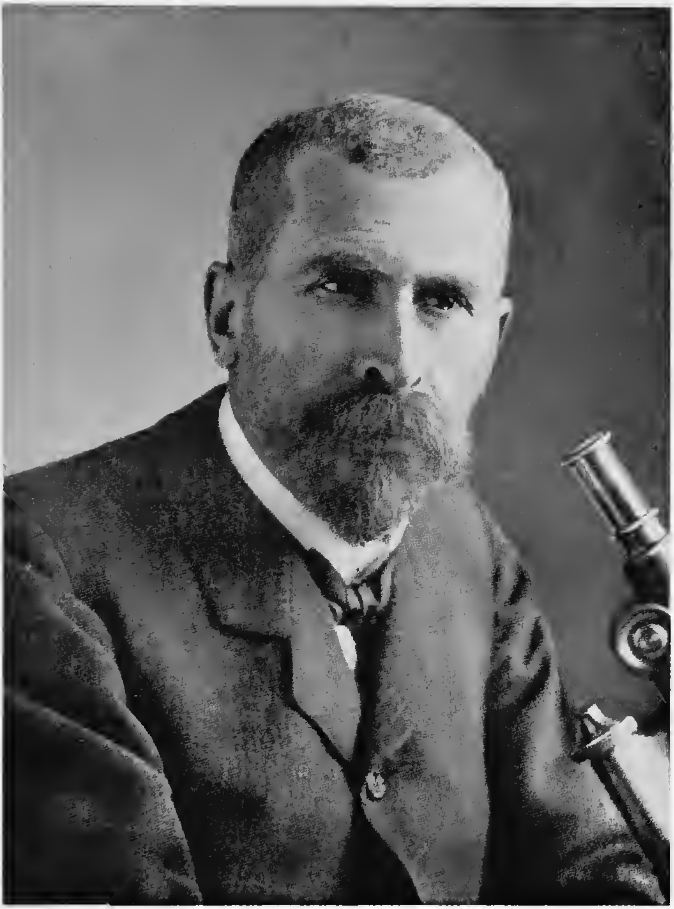
"Our researches on diphtheria and tetanus have led us to the question of immunity and cure in these two diseases: and we have succeeded in curing infected animals, and in immunising healthy animals so that they have become incapable of contracting diphtheria or tetanus."

The first cases treated with antitoxin were published by Behring, Kossel, and Heubner, in 1893. The antitoxin was first used in the Hospitals of our Metropolitan Asylums Board in November, 1894. To-day, we are able to look back over twenty years of continuous experience in every country of the world.

One of the earliest reports of results is in a paper, *Sérum-Thérapie de la Diphtérie*, published by Roux, Martin, and Chaillou, in the *Annales de l'Institut Pasteur*, September, 1894. In the Hospital for Sick Children in Paris, before the antitoxin was used, the death-rate in the diphtheria-wards had been as follows:

In 1890	...	55·88 per 100 cases		Average, 51·71.
" 1891	...	52·45	"	
" 1892	...	47·64	"	
" 1893	...	48·47	"	

Out of 3,971 children, 2,029 had died. Then, in 1894, came the use of the antitoxin Between February 1 and July 24, 1894, the number of children admitted to the diphtheria-wards was 448.



PIERRE PAUL EMILE ROUX

Membre de l'Académie de Médecine et de l'Académie des Sciences.
Directeur de l'Institut Pasteur.

Cases in which the Klebs-Loeffler bacillus was not found were set aside. So were 20 cases, that were dying on admission. That left 300, who were treated with antitoxin. Of these, only 78 died: that is 26 per cent.

At the Trousseau Hospital, the antitoxin was not in use. During February to June, 1894, the diphtheritic cases numbered 520. Of these, 316 died: that is 60 per cent.

The cases at these two Hospitals may be divided into those which did not require tracheotomy, and those which did. The death-rate among those which did not, was 12 per cent. at the Hospital for Sick Children, and 32 per cent. at the Trousseau Hospital. The death-rate among those which did, was 49 at the Hospital for Sick Children, and 86 at the Trousseau Hospital.

That was twenty years ago*: and, from then to now, that has been the world's experience with diphtheria antitoxin. Not that the method is perfect: not that the antitoxin may not cause a rash, and pains in the joints, and a rise of tempera-

* These old reports are useful: for no Hospital would dare, to-day, to behave as some of them did in 1894. Here is another old report, from the *British Medical Journal*, October 20, 1895: "The most striking confirmation of the value of antitoxin has been afforded where the supply ran short during an epidemic. In Baginsky's clinic, the interruption of the serum-treatment promptly raised the mortality from 15·6 per cent. to 48·4 per cent."

ture: not that its use, all over the world, in many millions of cases, has never caused a death.* No serum-treatment is perfect. Only, this we know, that diphtheria-antitoxin has by this time, taking one country with another, saved more than a quarter of a million lives. How could it do otherwise? For it is Nature's own remedy. A perfectly healthy and well-fed horse is gradually and painlessly immunised, with small doses of the toxin, so that its blood contains the antitoxin. The brewing of this antitoxin, this antidote, in the horse, is Nature's own method. The horse is then bled, and the serum of the blood is put, by means of a hollow needle, under the patient's skin. The patient, of course, down with diphtheria, is brewing his own antitoxin, in his own blood, as fast as he can: but the fear is, that the diphtheria-germs in him may be brewing toxin faster than he is brewing antitoxin. Therefore, the horse's antitoxin must be used, to reinforce the patient's antitoxin. That, we must all agree, is a thoroughly reasonable treatment. Only, it must be given immediately, a full dose of it. Here is a table, from the cases at

* It does not cause any sort or kind of paralysis. Post-diphtheritic paralyses are due to the disease, not to the treatment. They are the work of the toxin, not of the antitoxin. They occur, as in diphtheria, so in typhoid fever. See, for all this, Dr. C. J. Martin's evidence before the Royal Commission on Vivisection, vol. iii., p. 219.

one of the Hospitals of the Metropolitan Asylums Board. It proves the importance of giving the antitoxin at once, without delay, so soon as the disease shows itself:

Cases treated.	Day of Disease, on which Antitoxin was given.	Deaths.	Death-Rate per Cent.
235	First day	0	0·0
1,441	Second day	62	4·3
1,600	Third day	178	11·12
1,276	Fourth day	220	17·24
1,645	Fifth day or later	308	18·72

Here is a similar table, from the Biennial Report of the Chicago Health Department for 1904-5, page 137:

Cases treated.	Day of Disease, on which Antitoxin was given.	Death-Rate per Cent.
608	First day	0·32
2,063	Second day	1·66
2,802	Third day	3·64
1,496	Fourth day	11·03
1,034	Later	21·08

There is reason to hope, that Science will be able, in a very few years, to get rid, almost or altogether, of such defects as are in the present

method of fighting the disease. Meanwhile, let us be glad that whole legions of children have been saved from death. Nor is it only the saving of lives that we may be thankful for, it is also the prevention of misery:

> "Instead of the spectacle of a number of patients in great distress, with swollen necks and stuffed-up noses, fretful and crying, such cases are now quite the exception, and, in the few one does come across, the condition lasts for a comparatively short time. . . . It was quite unusual (before 1895) for a nurse to care to stay very long in charge of one of the diphtheria wards, because she found the work so depressing. But nowadays the diphtheria wards are perhaps the most popular in the hospital, a fact which is mainly owing to the change in the general aspect of the patients and the greatly reduced mortality."*

Among the experiences of the entire world, let us take one set of facts, in this country, which anybody can verify for himself or herself. The Hospitals of the Metropolitan Asylums Board receive three out of every four cases of diphtheria over an area of 121 square miles containing five millions of lives: thousands of cases every year: what these Hospitals do not know about diphtheria-cases is not worth knowing. They began the

* From a clinical lecture by Dr. Foord Caiger, Medical Superintendent of the South-Western Hospital. See the *Clinical Journal*, May 23, 1906.

antitoxin-treatment in November, 1894; but only 24 cases were treated before 1894 came to an end: let us start clear with 1895. For the years 1895-98, we have the evidence given on November 12, 1907, to the Royal Commission on Vivisection, by Professor Sims Woodhead, now Professor of Pathology at Cambridge. He superintended the preparation of antitoxin for the Board Hospitals, and very carefully watched and reported the results of its use, from 1895 to 1898. His evidence is of absolute authority:

"You see a patient almost livid, breathing heavily, with a very high temperature, in great discomfort, and unable to sleep. You give that patient a dose of antitoxin: and in three or four hours he is breathing easily, the skin is acting, and the patient is comfortable, and he goes to sleep. That, to my mind, is even more striking than any statistics that one can bring forward.

"I may mention that, in our experiments on animals, carried out in connection with the testing of the potency of the antitoxin, an enormous dose of toxin may be neutralised by a dose of antitoxin; and you may see that animal recover without turning a hair, if one may put it in that way: never losing its appetite, never losing in weight, but simply going on as would a normal animal into which no toxin has been introduced.

"We found that the more antitoxin was given in any Hospital, and the earlier it was given, the greater was the diminution in the mortality.

"Our medical men are using more and more antitoxin every year. The worse the cases are, the more anxious they are to give the antitoxin. I said before, the very best results are always obtained when the antitoxin is given at an early stage, before the poison gets a thorough hold of the patient and damages the tissues. If you can give it early, the death-rate from diphtheria should be practically *nil*.

"In 1895, we only supplied 1,200,000 units of antitoxin to the whole of the Hospitals under the Board: in 1896 we sent out 25½ million units: and in 1897 we sent out 60¼ million units."

The doses given, in these first years, were much smaller than the doses usually given now. In the Board's Report for 1911, p. 210, we find that the number of units sent out, in 1911, was 106,172,000. "It is calculated that on an average 17,328 units were used for each patient. The amount of antitoxin supplied, the number of cases treated, and the amount of antitoxin used for each patient, all show a considerable increase. . . . In addition to the supply to the Board's institutions, two hospitals not under the Board—viz., the Middlesex Hospital, and the Hospital for Sick Children, Great Ormond Street—were, as in previous years, provided with diphtheria antitoxin, the total amount taken by these Hospitals during 1911 being 1,000,000 units as compared with 700,000 units in 1910."

Some points in the recent Reports of the Metropolitan Asylums Board are of special interest:

1. "It has been suggested, that the decline in the mortality amongst cases of diphtheria, which followed the introduction of the antitoxin-serum treatment of the disease, might largely be accounted for by the inclusion of numbers of cases which were certified as diphtheria after the bacteriological test only. Therefore such cases have been shown, this year, in a separate column from those exhibiting the usual clinical signs of the disease. It is very satisfactory to find that, notwithstanding the exclusion of the bacteriological cases, the death-rate, calculated on the admissions, is still as low as 9·8, as compared with a rate of 30 per cent. before the introduction of antitoxin."—*Report for* 1909, p. 145.

2. "In connection with the mortality of diphtheria cases, we draw special attention to the rate per 1,000 of the estimated population.* For some years prior to 1893, it had been steadily advancing, notwithstanding occasional reductions, until in the year mentioned it had attained the very high figure of 0·76. Since 1893, however, the rate has fallen; and this fall has been coincident with the introduction and increasing use of the antitoxic serum treatment of diphtheria."—*Report for* 1909, p. 152.

3. "In August last, the Local Government Board issued an order empowering the Metropolitan Borough Councils to provide diphtheria antitoxin for the poorer inhabitants of their districts."—*Report for* 1910, p. xvi.

4. The Report for 1910 states, p. 131, that the

* Some of the "anti-vivisectionists" make very dishonest use of the Registrar-General's returns. So it may be as well to say here, that these returns do not throw the very least shadow of a shade of doubt on the value of diphtheria-antitoxin.

death-rate, calculated on the admissions, was, notwithstanding the exclusion of "bacteriological" cases, the lowest on record—viz., 7·7. It also gives tables, pp. 253, 254, showing the contrast between cases treated with antitoxin, and cases treated without antitoxin. Of course, *taking all forms of diphtheria together*, and thus including all the trivial cases, which did not want the antitoxin and therefore did not get it, the death-rate is lower among the cases treated without antitoxin. Taking the severe cases by themselves—the laryngeal cases and the tracheotomy cases—the death-rate is far higher among the cases treated without antitoxin. Here are the tables:

SUMMARY OF THE ANTITOXIN TREATMENT OF DIPHTHERIA, 1900–1909.

All Forms of Diphtheria.

Cases treated with Antitoxin.			Cases not so treated.		
Cases.	Deaths.	Mortality per Cent.	Cases.	Deaths.	Mortality per Cent.
50,405	5,609	11·1	6,831	206	3·02

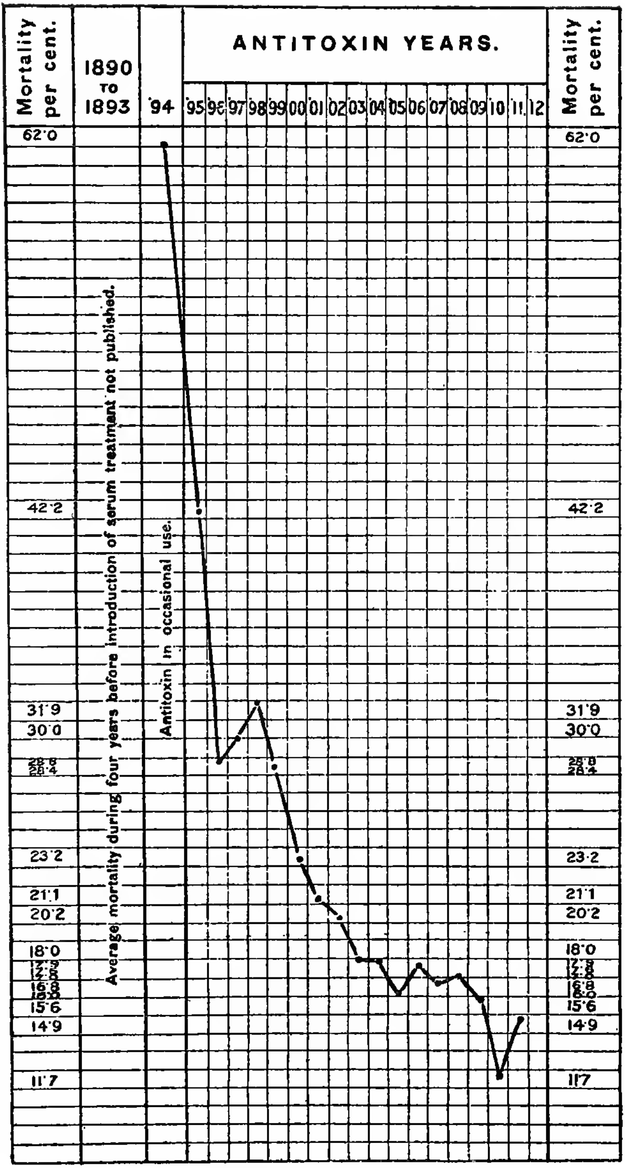
Laryngeal Cases.

Cases treated with Antitoxin.			Cases not so treated.		
Cases.	Deaths.	Mortality per Cent.	Cases.	Deaths.	Mortality per Cent.
7,445	1,358	18·3	129	74	57·2

Tracheotomy Cases.

Cases treated with Antitoxin.			Cases not so treated.		
Cases.	Deaths.	Mortality per Cent.	Cases.	Deaths.	Mortality per Cent.
3,128	965	30·8	59	51	86·5

5. The Report for 1911, p. 111, states that there was an increased prevalence, that year, of diphtheria:



LARYNGEAL DIPHTHERIA.

Metropolitan Asylums Board Hospitals. Report for 1911.

1,891 more cases were notified in 1911 than in 1910. The number of cases which were treated with antitoxin was 3,864. "The rate of mortality among cases treated on the first day of the disease was 2·7 per cent.; on the second day, 3·4 per cent.; on the third day, 8·9 per cent.; on the fourth day, 12·6 per cent.; and on the fifth day and later, 13·4 per cent."

6. A chart, from the Report for 1911, is reproduced on the preceding page. We are sometimes told that the blessings of diphtheria antitoxin must be discounted, because the disease, nowadays, is "of a milder type." But these laryngeal cases were not "of a milder type": they were all of them severe cases, every one of them.

7. The Report for 1912, p. 155, states that the death-rate, calculated on the admissions, was 6·8, the lowest on record. And it omits the usual antitoxin tables: for this good reason, that "the antitoxin treatment of diphtheria has been for some years past so well-established that further accumulation of details concerning it is unnecessary."—*Report for* 1912, p. 249.

Of late years, much study has been given, in this and other countries, to the important subject of diphtheria-carriers, *i.e.*, persons who have recovered from diphtheria, or have been in contact with diphtheria, and, though they are in good health, yet are capable of conveying the disease. A full account of the whole subject, from every point of view—historical, bacteriological, and practical—will be found in *The Carrier Problem in Infectious*

Diseases, by Ledingham and Arkwright (London, Edward Arnold, 1912).

Another important point is the use of the antitoxin to protect children who have been exposed to the disease. There is no doubt that this protective use of the serum tends to stop the spread of the disease, *e.g.*, in a school, or in a local epidemic: we have evidence, here, not only from our own country, but from France, Germany, and America. But the limits of this procedure are soon reached. Still, in some instances—such as might arise if one of a large family of small children were attacked by diphtheria—it might be well to protect the other children, if they had been much in close contact with the case.

X.

CHOLERA, PLAGUE, TYPHOID FEVER

CHOLERA

KOCH, in 1883, observed and described the germs of this disease: but it was not until 1892, the year of the Hamburg epidemic, that men of science, in all countries, were practically unanimous in their acceptance of his discovery.

Nothing, in all bacteriology, was more complex and laborious than the international work over Asiatic cholera. For there are many sub-species of these germs; and their variations, wide range of virulence, instability, and diversity of behaviour, are bewildering even to read of:—

"Variability of some degree is proper to all germs, as it is to higher animals and plants; but the cholera microbe is one of those in which, owing to their organisation and mode of life, that variability is particularly marked; so much so that not unfrequently, after an examination with all available tests, it is impossible to say whether the germ dealt with is, or is not, a representative of the cholera species."

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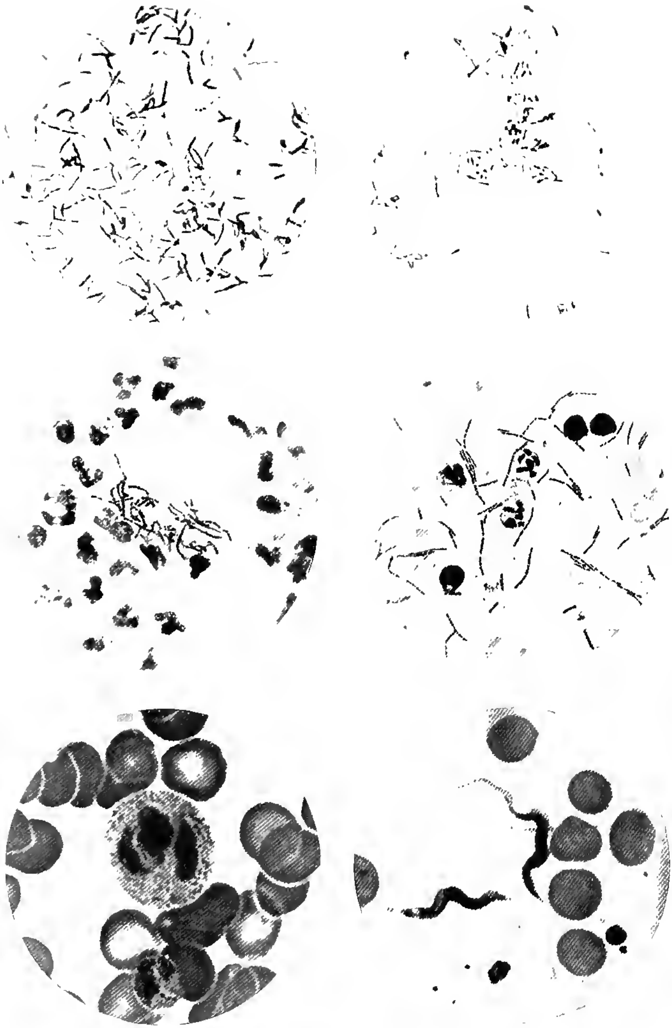
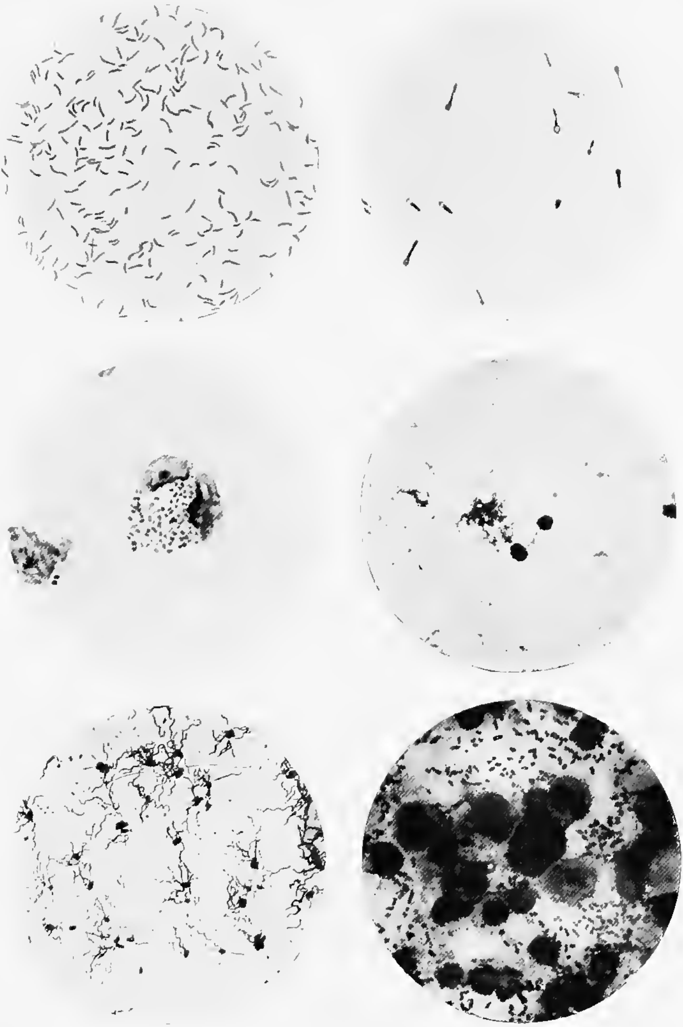


INFECTIVE DISEASES

1. TUBERCLE
2. DIPHTHERIA
3. STREPTOCOCCAL INFECTION
4. ANTHRAX
5. MALARIA
6. SLEEPING SICKNESS



7 8

9 10

11 12

INFECTIVE DISEASES

7. CHOLERA
8. TETANUS
9. EPIDEMIC MENINGITIS
10. MALTA FEVER
11. TYPHOID FEVER
12. PLAGUE

This statement, and the further statements on p. 113 and p. 116, are from Haffkine's monograph, *Protective Inoculation against Cholera.* (Calcutta: Thacker, Spink, and Co., 1913.)

Out of incessant observations, theories, experiments on animals, and experiments on self, came certain methods of protective treatment. Ferran's was the first: that was in Spain, in 1885. It was imperfect, in that he did not fully reckon with the variability and instability of the virus; nor did he so distribute his inoculations as to afford an exact estimate of their value.* In 1894, came the first use, in India, of Haffkine's method.

Haffkine, who now is Bacteriologist with the Government of India, began to study cholera in 1889, at the Pasteur Institute. He was only one of a great body of men of science occupied, in diverse parts of the world, on cholera: still, so far as it is reasonable to isolate one man's work, he is the man. The chief problems before him were—(1) To select, for his vaccine, the proper strain of

* "Absolument convaincu de l'efficacité de son procédé, Ferran eut le tort d'entreprendre d'emblée la vaccination en grand, au lieu de prouver d'abord le bien fondé de sa méthode par des essais portant sur des groupements limités, dans des conditions nécessaires pour permettre un jugement définitif. . . . Ceci explique comment, malgré les résultats, qui, dans leur ensemble, étaient sans aucun doute favorables à la vaccination, la méthode de Ferran n'eut que de très rares partisans et des adversaires nombreux."—Salimbeni, *Bibliothèque de Thérapeutique*, vol. xii., p. 411.

germs; (2) to decide the relation between virulence and immunising power; (3) to standardise his vaccine, and keep it steady at one degree of strength, as a *virus fixe.* Writing in 1913, he gives a summary of his work:

"The problem was eventually solved by reverting to the Vincenzi-Hüppe intraperitoneal injection and working out, from that starting-point, a plan which permitted the cultivation in animals of the germ of cholera, in a state of purity, indefinitely, generation upon generation; the raising of it to a well-determined degree of virulence, sufficient for the protection of man; and its maintenance at that level for an unlimited period of time, with the same certainty of result as obtains in the preparation of small-pox vaccine lymph and of Pasteur's antirabic virus."

His protective treatment was offered, in 1892, to the Russian Government, to be used in provinces then suffering from cholera: but the offer was declined, because of adverse reports of Ferran's method in Spain. At the end of 1893, having tested his vaccines on himself and others, "some sixty persons, mostly medical and scientific men interested in the solution of the problem," and found them harmless to health, Haffkine went to India, with a letter of commendation from our Government:

"In the course of the years 1892 to 1895, I submitted to study the effects of the above-described

two live vaccines, and inoculated, first, myself and a number of my personal friends, so that the reaction produced by the injection could be carefully observed, and its harmlessness established. Then I extended the operation to 42,197 persons inhabiting ninety-eight different localities in India —viz., in Bengal, Behar, the then North-Western Provinces and Oudh, the Punjab, the Brahmaputra Valley, and Lower Assam. In 1895-96 I inoculated a further 30,000 people in Bengal, Behar, Assam, the Central Provinces, and the Bombay Presidency. It was necessary to spread the operations in this manner, as it was not known exactly where cholera outbreaks might occur; while in some of the localities most threatened with such outbreaks—namely, in Bengal, where I carried out subsequently the most instructive of my operations—I was unable, for a considerable time, to obtain assent to my work. My efforts were directed to inoculating people under such conditions as would afterwards render possible an accurate study of results. In this manner I inoculated part of the officers, non-commissioned officers, and men in 64 British and native regiments; a proportion of the coolie population in 45 Tea Estates in Assam, Cachar, Sylhet, and the Chittagong district; part of the inmates of boarding-schools and orphanages, and of 9 civil jails; the population of a supervised village of Sansis (one of the criminal tribes) near Sialkot, Punjab; inhabitants of Himalayan villages situated along the Hardwar pilgrim route, between Naini Tal and Mussoorie, and liable to become infected with cholera; residents of the suburban quarters (*bustees*) of Calcutta, and so on. Elaborate arrangements were made among these communities for

recording cholera occurrences for a certain period to come; and by 1896 a mass of material was collected."

That is the way to judge the worth of a protective treatment. There must be, in one and the same community, during one and the same epidemic, lives protected and lives non-protected: and these two sets of lives must be alike in everything else—food and clothing and health and habits and surroundings. Then, let Nature decide. Put the problem, fairly and squarely, to her. Offer to Nature, for a demonstration, tenement-houses, jails, tea-gardens, regiments, boarding-schools, villages; and follow carefully the result. Nature demonstrated, very clearly, that the protected were indeed protected against cholera. Out of many examples, take the results in Calcutta, and on the Cachar Tea Estates.

Calcutta.

From 1894 to 1896, the work in Calcutta was supervised by Dr. W. J. R. Simpson, C.M.G., now Professor of Hygiene in King's College, London, then Health Officer of Calcutta. The service was under the direction of the Municipal Health Office. The utmost strictness of inspection, visitation, and analysis of cases, was maintained.

From the end of March, 1894, to the end of

December, 1896, in Calcutta, 7,908 persons were inoculated, mostly in the cholera-stricken suburbs. Cholera, later, visited 85 houses, in which protected and non-protected persons were living together, and 1 ship, on which some of the crew were protected. The total number of inhabitants in these houses, and on this ship, was 1,395. Among the protected, some had received only a preparatory "vaccine I.": some had received both vaccine I. and vaccine II. Among the latter, only *one* instance of failure was observed: and that was 688 days after the date of inoculation.

Of the 85 houses, 5 must be left out of the reckoning, because the proportion of protected persons in them was less than 1 to 10 of the not protected: thus, the escape of the protected might be due to mere chance. (These five households contained 161 not protected, 5 of whom were attacked, and 7 protected, none of whom was attacked.) That leaves 80 houses and 1 ship. But, in 2 of the 80 houses, cholera broke out twice: each of these houses thus comes twice into the reckoning. That gives us 82 houses and 1 ship. Here is Haffkine's comment on the table of cases —or, one ought to say, Nature's comment:

"This table at once reveals the fact that the incidence of cholera among the inoculated varied according to three periods. During the first 4 days

after the date of inoculation, cases were observed both among the inoculated and the non-inoculated. After the first 4 days, there was a period of nearly 14 months (412 days), in which 3 attacks occurred among the inoculated, while among the non-inoculated, in the same houses, cases were taking place at short intervals throughout the whole of that period. And from the 417th day, during the remaining thirteen months of observation, cases reappeared among the inoculated.

"During the immunisation period, which occupied 4 days, the number of deaths among the inoculated was 1·39 times smaller than among the non-inoculated.* During the period of immunity, lasting 412 days, the number of deaths among the inoculated was 15·79 smaller than among the non-inoculated:† which is to say that of every 100 deaths from cholera, which were to take place in that period of 412 days, 94 could be averted by the use of the vaccine. Lastly, during the third period, from the 417th to the 800th day—when the effects of the immunisation had vanished—the number of deaths among the non-inoculated was 1·23 times smaller than among the inoculated."‡

* In the 12 houses, and the ship, where cholera occurred during these 4 days, there lived 123 non-protected, and 142 protected. The 123 had 10 cases, of whom 6 died. The 142 had 6 cases, of whom 5 died.

† In the 54 houses where cholera occurred during these 14 months, there lived 539 non-protected, and 279 protected. The 539 had 66 cases, of whom 61 died. The 279 had 3 cases, of whom 2 died.

‡ In the 16 houses where cholera occurred during this period, there lived 126 non-protected and 41 protected. The 126 had 17 cases, of whom 15 died. The 41 had 6 cases, all of whom died.

Cachar Tea Estates.

The work on these Estates was supervised by Dr. Arthur Powell. Strong doses of vaccine II. were used. The inoculations were made during 1895-96. Observations were continued till the end of 1899. On these Estates, protected and non-protected lived together, in huts belonging to the Estates. The labourers were registered, and supervised daily: thus, all incidence of disease would be known at once.

Among 6,549 non-protected coolies, there were 198 cases, of whom 124 died.

Among 5,778 protected coolies, there were 27 cases, of whom 14 died.

These two instances may suffice. Other references to the treatment, in Russia, Japan, Persia, Batavia, and Manila, will be found in Haffkine's monograph. In India—though some very good results were lately published—the ravages of plague have delayed cholera-work: and the question is not yet decided, whether the use of a devitalised vaccine can be trusted to give results equal to those obtained with a live vaccine.

Plague.

In 1894, Kitasato and Yersin,* working at plague in Hong-Kong, discovered the *bacillus pestis* (see the *Lancet*, August 11 and 25, 1894). Thus, 1894 stands out as the first year of diphtheria antitoxin, the first year of Haffkine's protective inoculation against cholera, and the first year of the bacteriology of plague.

Lovers of the *Vie de Pasteur* will remember the account of the little festival at the Pasteur Institute in April, 1895. The occasion was the Centenary of the Ecole Normale: it was five months before Pasteur's death: he had lost all bodily strength, but was able to receive some old *Normaliens.* In the great laboratory, Roux had arranged an exhibition of the work of near forty years: the original flasks used by Pasteur in 1860, ferments, bacteria, everything, down to pure cultures of diphtheria and plague:

"Vers midi, Pasteur se fit transporter dans le laboratoire. M. Roux, prenant un microscope, montra à son maître le bacille de la peste. En voyant tant de choses représentatives de ses propres travaux et des recherches de ses élèves, Pasteur pensait aux disciples qui, de tous côtés, poursuivaient l'œuvre commencée. En France, il

* Yersin is now Director of the Pasteur Institutes at Nhatrang and Saigon, and Surgeon-in-chief to the French Colonial Forces.

venait d'envoyer à Lille le Dr. Calmette qui allait, en quelques mois, créer de toutes pièces un nouvel et admirable Institut Pasteur. Le Dr. Yersin en Chine continuait sa mission. Un normalien, entré dès seize ans le premier à la grande Ecole et devenu préparateur au laboratoire, M. Le Dantec, était au Brésil où il étudiait la fièvre jaune dont il faillit mourir. Le Dr. Adrien Loir, après une longue mission en Australie, dirigeait un Institut Pasteur à Tunis. Le Dr. Nicolle organisait un laboratoire de bactériologie à Constantinople. *Ah! que de choses encore à faire!* disait Pasteur d'une voix affaiblie en serrant affectueusement la main de M. Roux."

From the discovery of the cause of plague, came the discovery of the transmission of plague, by rat-fleas, from rats to man.

*The Transmission of Plague.**

Plague, after long absence from India, flared up in Bombay, in October, 1896. It is estimated that 20,000 died in 9 months:

"The scenes witnessed by those whose business took them to the plague-infested parts of the city were heartrending beyond description. Streets deserted, whole families found dead with no record

* For general study of this subject, it would be hard to find a better guide than the pamphlet *Plague in India, Past and Present: A Contrast*, by Surgeon-General Bannerman, I.M.S., Director of the Plague Research Laboratory of the Government of India. Issued by the Research Defence Society, 1910.

to tell who they were or where they came from, mothers lying cold with helpless babies beside them whom no one dared pick up to take care of. . . . Thousands of pounds were wasted on disinfectants, which experiment has since shown are utterly useless, and innumerable lives were lost through ignorance of the proper precautions to adopt. . . . It was only after years of observation and of laboratory experiments that it was discovered how plague really spreads.

"As time went on, and epidemic succeeded epidemic, it gradually came to be realised that the principal agent in the start and spread of plague among men was the rat. *No rats, no plague*, passed into a sanitary byword, and the common people came to regard dead rats as a species of omen, and a warning to quit the houses where they were discovered. . . .

"The Plague Commission, sent out from England in 1898 at the request of the Indian Government, came to the conclusion that the infection of plague always entered through the skin.

"About the same time, a French observer made experiments which tended to incriminate the flea, though the results of his researches were by no means conclusive. A young officer of the Indian Medical Service was, however, so convinced, by a study of the facts brought to light by the experiences of successive epidemics, that there was something in this theory, that he proceeded to study the rats of Bombay, and the insects parasitic upon them. He discovered that the flea found on rats is of a different species from that infecting man; but that if the rats were removed by disease or otherwise, their fleas would take to man and feed

upon him. He discovered by experiment that fleas fed on plague-stricken animals contained plague germs in their stomachs in a living state, and that the germs freely multiplied there. He likewise found that a proportion of the guinea-pigs he exposed to the bites of these insects developed plague, and died of it. . . . At this stage in the investigations, the Government of India appointed a second Plague Commission, composed of bacteriologists from the Lister Institute, associated with an equal number from the Indian Medical Service."—Bannerman.

The Commission set to work, with observations innumerable and experiments of great ingenuity. They ascertained that neither contaminated food nor contaminated soil was responsible for the spread of plague in India. Slowly they drew the chain of proof round the rats and the fleas. For example, there was the tenement-house in Bombay, "where some hundred people lived in a number of small rooms. Rats died in the tenement, and living rats disappeared. Two days after, the inhabitants were so troubled with fleas that they had to forsake their rooms and sleep in the verandahs. A few days more, and plague appeared among them. A search for fleas on the people revealed the interesting fact that a large proportion of the capture were rat-fleas, and that some of them contained plague-germs in their stomachs."

There is not space for a full account of the ex-

periments: but the following examples will show the lines on which the work was carried out:

1. Two cages were placed in a glass box, inaccessible to fleas from outside. In cage A was put a rat artificially infected with plague; and from 10 to 20 rat-fleas were put with it. When the rat died, a healthy rat was put in cage B. With healthy rats, specially imported from England, and therefore above suspicion of previous exposure to plague, 11 out of 16, put in cage B, got plague. To exclude the possibility of aerial infection, healthy English rats were exposed not to plague-rats, but only to fleas from plague-rats: and 8 out of 13 died.

2. Small rooms were so constructed as to be "flea-proof." All animals put in them were carefully searched, to make sure that they had no fleas. Fifty guinea-pigs were put in a flea-proof room, 7 feet by 6 feet, and ten artificially infected guinea-pigs were put with them. The room was purposely not cleaned out, so that, in a few days, the animals were living in most insanitary conditions. As the infected guinea-pigs died of plague, the bodies were left for twenty-four hours before removal, so as to afford every chance for contagion to play its part. Yet not one of the fifty healthy animals died.

3. Five infected guinea-pigs were put in a room, died of plague, and were removed. Then twenty-

five healthy guinea-pigs were put in: plague at once broke out among them, and all died. Fleas were present in great numbers throughout this experiment. These fleas were transferred to a room where fifty guinea-pigs had been living for three weeks. Plague broke out among them, and all died.

4. Animals in cages hung above a flea's jump from the floor invariably escaped plague: animals in cages hung lower did not.

5. Guinea-pigs were let run free in rooms from which plague-cases had been removed to Hospital. Next day, the fleas were chloroformed off the guinea-pigs, and counted. It was found that nearly all of them were rat-fleas, in large numbers. Many of the guinea-pigs developed plague.

6. Animals were hung in cages, in plague-infected rooms; some of the cages were made to exclude fleas, some were made to admit them. None of the cages touched the floor, or could be reached by rats. In 122 such experiments, none of the animals in the flea-proof cages got plague, but 17 in the other cages did. Of 401 counted fleas, the majority were rat-fleas. Of 132 dissected rat-fleas, 26 had plague-germs in their stomachs.

7. In 1907, houses under observation in Bombay were divided into A, those known to be plague-infected: B, those presumably plague-infected:

and C, those known not to be infected. By setting "guinea-pig traps" in these three classes of rooms, it was found that class A furnished nearly three times as many fleas as class B, and twelve times as many as class C.

8. Monkeys, put under similar conditions of experiment, were found just as liable as guinea-pigs to infection.

9. A chart, showing the number of plague-infected rats found among the hundreds daily killed in Bombay during an outbreak of plague, and the number of human plague deaths during the same period, showed, very clearly, that the infection goes from rats to man.

Thus, by experiments, observations, and sanitary methods, all working together, year in year out, the transmission of bubonic plague, by rat-fleas, from rats to man, was discovered and proved. "These discoveries," says Bannerman, "provide us, for the first time, with a sure and scientific basis on which to work, and have explained the cause of failure of the well-meaning efforts to combat the disease which were made when plague first appeared. Efforts are now concentrated on the breaking of the chain of events leading from the rat through the flea to man."

Then he goes on to estimate what hope of success attends these efforts. What can be done?

Something, here and there: more, in course of time: but the difficulties are colossal. Possibly, the final salvation of India from plague may come not from man, but from Nature: it is not impossible that future generations of rats should be born immune against plague. The terror of plague is just in this fact, that it is, strictly speaking, not a disease of man, but a disease of rats.*

Serum-Treatment of Plague.

The first use of this treatment was by Yersin, in 1896, in Canton and Amoy. That the serum, when it is used for *protection* against plague, is valuable, nobody doubts: but this protection lasts only a very short time.† Used for the actual *treatment* of plague-stricken patients, it gave good results in China; but the results in India were not well marked. Against that worst type of the disease, pneumonic plague, which is contagious from man to man, neither serum nor any other treatment is of much use.

* "Il ne faut pas oublier, en effet, que la peste n'est qu'accidentellement une maladie humaine."—Dujardin-Beaumetz, *Bibl. de Thér.*, xii., p. 462.

† "Chez l'homme, l'efficacité du sérum antipesteux employé préventivement n'est plus à démontrer, et tous ceux qui l'ont utilisé de cette façon sont d'accord sur ce point; mais cette action presque immédiate n'est que passagère et, après une dizaine de jours, toute immunité a disparu, et l'individu, n'étant plus sous l'influence sérique, est à la merci d'une atteinte pesteuse, s'il ne prend la précaution de recourir à une nouvelle injection de sérum."—Dujardin-Beaumetz.

Protective Vaccine against Plague.

Haffkine's protective vaccine was first used on man in January, 1897. It is a devitalised vaccine: the *bacillus pestis* is grown in sterilised broth, and then is killed by heating: and the fluid, with a trace of carbolic added, is put up in hermetically sealed phials:

"In popularising the plague prophylactic, the one difficulty that has to be fought against consists in overcoming the popular idea that it is the living virus of plague that is injected. Medical science has to contend sometimes, even in England, against credulous readiness to believe evil of others. What it has to contend with in India, may be judged of by the fact that, when inoculation against plague was started in the Punjab, it was popularly believed that the doctors were being sent round to propagate plague, in order that human livers might be available, with which to make a potent drug that could renew the youth of the Empress, whose Diamond Jubilee had recently been celebrated!

"Yet, in spite of such ideas, the total demand for the prophylactic continues slowly to increase; its protective power is found to be so marked, wherever it is put to a practical test."—Bannerman.

Haffkine, having proved on rabbits, past all possibility of doubt, the efficacy of his vaccine, inoculated himself, on January 10, 1897, with a fourfold dose: then Colonel Hatch, Principal of

the Grant Medical College, Bombay, and other members of the College staff.

On January 23, plague broke out in the Byculla Gaol, Bombay. Between January 23 and January 30, there were 14 cases, of whom 7 died. On the afternoon of January 30, the protective vaccine was given to 152 prisoners: and 172 were left unprotected. The outbreak came to an end on February 7. The 152 protected had 1 case, who recovered. The 172 not protected had 7 cases, of whom 2 died. Similar results were obtained in Undhera, Bombay, Kirki, Belgaum, Khandesh, Hubli, Nagpur, Dharwar, and Karachi. Not that the work was perfect: it had to be done under very severe pressure: and, at this or that point, it broke under the strain. But the fact remains, that thousands of lives were saved. Take the Empress Mills at Nagpur: 1,116 protected, with 6 deaths: 2,663 not protected, with 179 deaths. Take the houses visited by plague in Undhera: 71 protected, with 3 deaths: 64 not protected, with 26 deaths. Take the Punjab villages: the figures are on a grand scale: 186,797 protected, with 814 deaths: 639,630 not protected, with 29,623 deaths.

Or take, not any elaborate statistics—for we all know the old gibe about statistics proving anything—but take the word of the men and women who bore the burden and heat of the day: who

slaved their strength away, and risked their lives, over the work, like Dr. Alice Corthorn, who herself inoculated some 75,000 patients: or take the little personal experiences—such as Major Forman told to the First Plague Commission—"Of my private servants there were in all, including their wives and children, 28 people inoculated. There have been no cases of plague and no deaths up to date. There were 3 uninoculated. One was a child of nine years old, whose father refused to allow it to be inoculated. It died of plague 12 days after the other people were inoculated. The other 2 cases that were not inoculated were not so distinctly under my own observation. One was a sweeper employed in the cantonment, and sleeping in my compound; he, I am told, died of plague some months afterwards. The other was my water-carrier: he threw himself into a well: I was informed that he had buboes and fever, and ran away to escape segregation. Of the 28 inoculated, none died of plague: and of 3 uninoculated, 2 are said to have died of plague, and 1 undoubtedly died of plague."

Typhoid Fever.

The bacteriology of typhoid (enteric) fever dates from the discovery, in 1880-81, of the germs of the disease, the *bacillus typhosus* of Eberth. Then

came many years of laboratory work: then, the results of that work in practice. The discovery of Widal's reaction; the discovery of protective inoculation; the anti-typhoid campaign led by Koch in Germany; the recognition, in all countries, of the risk from typhoid-carriers; and the study of para-typhoid fever—all these great lines of research have been followed by a multitude of workers: but there is not room here for more than a short note on protective inoculation.*

Protective Inoculation.

The name of Sir Almroth Wright stands first, all the world over, for this method of treatment: but many names are memorable — Sir William Leishman and Major Harrison in India, Major Russell in America, Pfeiffer and Kolle in Germany, Chantemesse and Vincent in France: these, and many more.

The first use of the treatment in our country was in July–August, 1896, at Netley Hospital, by Wright and Semple, on 18 men who tried it on themselves†:

* For further reading, no better guide—one might almost say, no better reading—could be found than Ledingham and Arkwright on *The Carrier Problem.*

† See *Lancet*, September 19, 1896, and *Brit. Med. Journ.*, January 30, 1897. In Germany, about the same time, Pfeiffer and Kolle published cases treated. See *Deut. Med. Woch.*, November 12, 1896.

"A good deal of fever was developed in all cases, and sleep was a good deal disturbed. These constitutional symptoms had to a great extent passed away by the morning, and laboratory work went on without interruption. . . . With two exceptions, all these vaccinations were performed upon Medical Officers of the Army or Indian Medical Services, or upon Surgeons on Probation who were preparing to enter those services."

The first use of the treatment in the actual presence of an outbreak of typhoid was at the Kent County Asylum, October, 1897. Before the inoculations were undertaken, 12 cases had occurred among the staff, which numbered about 200. The group under observation was nurses and attendants, 200 in all; 84 protected, 116 not. The protected had no cases: the non-protected had 4. During 1899, while Wright was with the First Plague Commission in India, the treatment was given to many of our Army. The group under observation —regiments and other units of the British Army in India—was 30,353 persons, of whom 4,502 were protected, and 25,851 were not. The protected had 44 cases, with 9 deaths: the non-protected had 657 cases, with 146 deaths. Later in 1899, came the instance of the 15th Hussars, at Meerut: 360 protected had 2 cases, with 1 death: 179 non-protected had 11 cases, with 6 deaths. In 1900, came the very favourable instances of the British

Garrison in Egypt and Cyprus, and of the patients in Richmond Asylum, Dublin.

In October, 1899, began the War in South Africa. Here, we have Colonel Simpson's *Medical History of the South African War*, and the Report, after the War, of the Committee on Field Sanitation. The protective treatment, in 1899, was still an imperfect instrument: it was put to a very severe test, under conditions of terrible hardship: we may fairly wonder, not that it did not achieve more, but that it achieved so much. The figures given by Colonel Simpson will be found over-page.

Sir William Leishman, after a critical commentary on the results obtained in the War, and on certain factors unfavourable to the success of the treatment, says, "It is noteworthy that, in spite of all these factors, the general analysis of the results should show that typhoid was twice as common in the non-inoculated as in the inoculated, and, in my opinion, it is even more striking that, in every corps, without exception, the ratio should have been in favour of inoculation."

It is fifteen years since the South African War: let us take some events of less age. The Government of the United States, in the autumn of 1911, made the treatment compulsory, in the United States Army, on all officers and men under forty-five years

Corps.	Strength Embarked.			Inoculated.		Non-inoculated.		Mortality per 1,000.	
	Total.	Inoculated.	Non-inoculated.	Cases.	Deaths.	Cases.	Deaths.	Inoculated.	Non-inoculated.
Household Cavalry	694	104	590	10	0	192	35	—	59·3
Cavalry	20,625	1,491	19,134	107	4	4,384	617	2·6	32·2
Imperial Yeomanry	35,170	1,508	33,662	162	22	4,759	643	14·5	19·1
Royal Artillery ...	19,636	1,265	18,371	150	11	3,931	546	8·6	29·7
Royal Engineers ...	7,871	677	7,194	66	12	1,540	234	17·7	32·5
Guards	11,575	976	10,599	140	12	2,015	284	12·2	26·7
Infantry	215,129	6,523	208,606	537	72	28,409	4,120	11·0	19·7
C.I. Volunteers ...	1,666	935	731	81	16	131	23	17·1	31·4
Army Service Corps	5,911	74	5,837	8	1	1,391	205	13·5	35·1
R.A.M. Corps ...	8,634	1,030	7,604	154	13	1,745	234	12·6	30·7
Army Ordnance Corps	1,333	43	1,290	2	0	257	50	—	38·7
Totals and Average Ratios	328,244	14,626	313,618	1,417	163	48,754	6,991	10·0 ±1·2	32·3 ±2·0

old—excluding, of course, those who had already had typhoid. The total number for treatment was 76,000: the number already treated, without compulsion, was 17,000. The French Senate, in the winter of 1913, passed a Bill making the treatment compulsory in the French Army: and, in special circumstances, among reservists.

In Avignon, in the summer of 1912, there was typhoid in the barracks. Of 2,053 men, 1,366 were protected, and 687 were not. It is on record—hard to believe, but there it is—that, though the non-protected, the minority, had 155 cases with 21 deaths, the protected, the majority, had not one case.

For our Army in India, we have the Report, October, 1912, of the Anti-Typhoid Committee appointed by the Army Council:

"The histories, as regards typhoid fever, of 19,314 soldiers, whose average period of service abroad was 20 months, were carefully followed, and every precaution possible was taken to verify the diagnosis bacteriologically. Of this number, 10,378 were inoculated, and 8,936 not inoculated. The case incidence of typhoid fever among the inoculated was 5·39 per 1,000, and among the non-inoculated 30·4 per 1,000.

"There is no reason for supposing that this difference can be attributed to a want of homogeneity between the two groups. The age distribution among inoculated and non-inoculated was

practically the same. They were intermingled and lived under identical conditions.

"The experience of Lieutenant-Colonel Sir W. B. Leishman and the inoculating officers lends no support to the view that soldiers who, from their character and habits, might presumably be more likely to incur the risk of infection, present themselves for inoculation in smaller numbers than their more careful comrades.

"In the opinion of the Committee the substantial difference in the incidence can only be attributed to inoculation."

The Committee make two recommendations. One, that research-work on the treatment should be continued: the other, that

"Every measure which may be considered practicable should be employed to extend the practice of anti-typhoid inoculation in the Army. In the opinion of the Committee its universal application is desirable."

Sir William Leishman, in a letter which has just been issued from the War Office to the medical profession, appeals to them to support strongly the efforts which the Army Medical Department is now making to secure the anti-typhoid protection of our Territorial Force:

"The benefits of inoculation are so well recognized in the regular forces that we find little difficulty, in foreign stations, in securing volunteers for inoculation; for instance, about 93 per cent. of

the British garrison of India have been protected by inoculation: and typhoid fever, which used to cost us from 300 to 600 deaths annually, was last year responsible for less than 20 deaths.

"Inoculation was made compulsory in the American army in 1911, and has practically abolished the disease. In 1913, there were only 3 cases and no deaths in the entire army of over 90,000 men."—*British Medical Journal*, August 22, 1914.

A very notable instance of the value of anti-typhoid treatment was published in the *British Medical Journal* of June 6, 1914: "In the Canadian Pacific Railway camps in the province of Alberta, anti-typhoid vaccination has been extensively carried out of late, under the direction of Dr. H. G. Mackid. The results have been most encouraging; for, in 1911, among 5,500 men who were inoculated, 2 only contracted typhoid, while of 4,500 who had not been treated, 220 fell ill with the disease. In 1913, 8,400 men were vaccinated, and only one case of typhoid occurred amongst them; moreover, it is probable that the man was ill at the time of vaccination. During the same year, among 2,000 men who were not inoculated, 76 cases of typhoid occurred."

XI.

MALTA FEVER, MALARIA, YELLOW FEVER

THIS book, though it is a book of omissions, is already longer than the standard set for it: but some sort of note must be put here on those researches into Malta fever, malaria, and yellow fever, which have done so much for the health and wealth of nations.

MALTA FEVER.

Sir David Bruce, in his evidence before the Royal Commission on Vivisection, November 5, 1907, gives a full account of the stamping out of this disease. It is less fatal than typhoid, but more severe: more tedious, more painful. It is widespread over the tropical and sub-tropical regions of the earth. In 1886, Bruce proved, past all doubt, that certain germs, the *micrococcus melitensis*, are the cause of the fever. Unhappily, this discovery was not followed up till many years later. In 1904, the Malta Fever Commission set to work, to discover the source of the infection:

"At the time this work began, everybody supposed that Malta fever was due to effluvia, that it was due to this minute micro-organism finding its way into the air of wards from the sick, or into the air of rooms from drains, sewers, etc., and so causing infection. . . . At one time it was thought, for example, that the Grand Harbour of Malta was the breeding-place of this fever."

Many researches, therefore, were made on hospital-air, on the Harbour-water, on dust, and so forth:

"It was found, from these experiments, that the *micrococcus* was not conveyed either by the air, or from the effluvia, or from the Harbour-water; nor from dust collected in suspicious places where one might hope to find it, contaminated places; nor from the air and dust, for instance, of fever wards, or of rooms where cases of the fever had occurred, and so on. All these experiments were negative."

Then began the gradual tracking-down of the infection to the goats' milk:

"It was discovered, by animal experiment, that infection could be conveyed by the mouth. This discovery came, as it were, by an accident, at the end. In an investigation of this kind, you naturally examine all the animals round about, in order to find out if any of them harbour the disease. The goat was looked upon by us as the most refractory and the most unsusceptible animal we could imagine. We do not consider that the goat is readily susceptible to human diseases; it does not even take tuberculosis, which is such a common

animal disease; so that we look upon the goat as the animal that is about farthest away from taking a human disease; and, as only the monkey took this disease, and not the rabbit, guinea-pig, rat, or dog, we considered that it was very improbable that a goat would take it.

"But, as a matter of routine, some goats were taken and inoculated under the skin with the *micrococcus melitensis*, and some were also fed on a small quantity of the culture—that is to say, a little of this *micrococcus melitensis* is taken out of a tube and put on the food, so that the animal eats it. These animals were examined afterwards as to their temperature and general appearance. But nothing happened."

But their blood, tested by Widal's test, gave a positive reaction. That is to say—

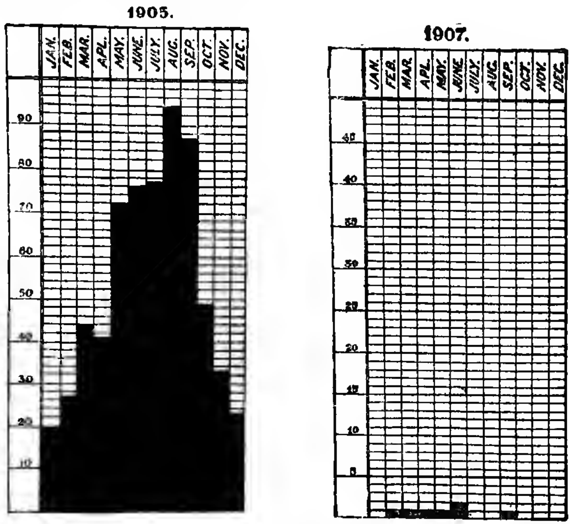
"The goats did not get the fever in the way that we consider characteristic of fevers. They got the fever, but did not show any external manifestations of that fever. The micro-organism did multiply in their bodies, but it did not give rise to any ill-health: it did not give rise to any fever. By looking at the goat you could not say that that goat was ill. It gave as much milk as a perfectly healthy goat; it was as fat and smooth-looking as a healthy goat. So that it was only by this blood-examination that it was suspected that something was occurring. We suspected that the stuff we put in had not died off—as ordinary non-pathogenic organisms would, when brought into contact with a non-susceptible animal—but that it had gained some ground, and was multiplying to some extent."

In June, 1905, light was thrown on the problem of Malta fever:

"More goats were bought: and before injecting them or before feeding them, their blood was examined, as a matter of routine, to see that the blood was all right. And curiously enough, goats bought at this time showed this same Malta fever reaction. And then the idea struck us, that the goats, the ordinary goats of Malta, might be suffering from this fever. And, on examining the blood of these ordinary Maltese goats, the *micrococcus melitensis* was found in it: and on going further, and examining the milk of these apparently healthy goats, a certain percentage of them were found to contain that *micrococcus melitensis* living in their milk. And that, of course, threw a great flood of light at once on the whole question.

"That was the important discovery, because it at once explained various things in the epidemiology of the disease—that seasonal prevalence had little or nothing to do with it: that whether it was a large town or small village, nothing in different methods of sanitation seemed to matter—the curious fact that officers were much more struck by this fever than the privates was also explained. And, after more work, the Commission came to the conclusion that the only way that a man takes Malta fever in Malta is by the drinking of goats' milk. Perhaps once in a thousand times, he may take it in some other way; but you can sweep all that aside: the drinking of goats' milk is the main path of infection. And naturally, of course, it is easy to stop to a great extent our sailors and soldiers drinking goats' milk. So that, when the

thing was once brought to the attention of the authorities, at once the disease was blotted out of the garrison of Malta."



MALTA FEVER: BEFORE AND AFTER THE PROHIBITION OF GOATS' MILK.

On July 1, 1906, the use of goats' milk was prohibited, by official order, to our men in Malta. The admissions into hospital had been 404 in 1903, 320 in 1904, and 643 in 1905: and, in 1905, no less than 403 officers and men had been invalided home. In 1906, up to July 1, there were 123 cases: during the rest of 1906—including the worst months for the fever—there were 40 cases. In 1907, 11 cases: in 1908, 5 cases: in 1909, 1 case.

MALARIA : YELLOW FEVER.

It was in 1880, that Laveran, a French Army-Surgeon in Algeria, first saw the *plasmodium malariæ*, in the blood of one of his patients.* In 1894, Sir Patrick Manson set to work on the theory of the transmission of malaria from man to man by the mosquito. In 1895-96, came the work of Sir Ronald Ross, and of MacCallum. By 1898, Ross had discovered and proved the whole cycle of the development of *plasmodium malariæ;* how it must go through a phase of changes in the mosquito, before it is put back into human blood. In 1899 and 1900, many Expeditions were sent out, from diverse countries. In 1900, also, among many voluntary experiments on man, were those made at Ostia and in London :

1. From June to October, throughout the "malarial season," a mosquito-proof hut was

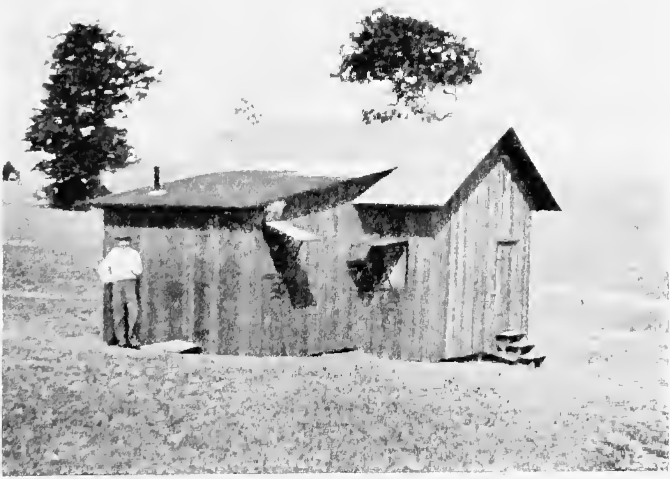
* "Le 6 novembre, 1880, j'examinais le sang d'un malade en traitement pour fièvre intermittente à l'hôpital militaire de Constantine, lorsque je constatai pour la première fois l'existence de filaments mobiles qui adhéraient aux corps pigmentés et dont la nature animée n'était pas douteuse. J'eus à ce moment même l'intuition que j'étais en présence des véritables microbes du paludisme."—Laveran, *Traité des Fièvres Palustres*, 1884. It is to be noted, moreover, that he says: "Les moustiques jouent-ils un rôle dans la pathogénie du paludisme comme dans celle de la filariose? La chose n'est pas impossible: il est à noter que les moustiques abondent dans toutes les localités palustres."

erected near Ostia, on water-logged land saturated with the fever. In this hut Dr. Low, Dr. Sambon, and others, lived, without taking a grain of quinine: they merely kept off the mosquito with wire screens and mosquito-curtains. Not one of them had any touch of the fever, though it was all round them.

2. Mosquitoes, after biting a malaria-patient in Rome, were forwarded, by the British Embassy, to the London School of Tropical Medicine: and Dr. Manson and Mr. Warren let themselves be freely bitten. In due time, they had malarial fever; and the *plasmodium* was found in their blood.

The experiment at Ostia coincides, in time and in plan, with the work done at Camp Lazear on yellow fever. Finlay had proved, so far back as 1881, that yellow fever may be conveyed, by the mosquito, from man to man. In 1900, the Government of the United States sent a Commission to study yellow fever in Havana. The Commissioners (Walter Reed, Carroll, Lazear, and Agramonte) made use of an Army Camp, strictly isolated. They erected a hut of two compartments, separated by a fine-meshed wire screen. In the one compartment were mosquitoes, infected from a case of yellow fever: their infectiveness had been proved by a voluntary act of self-experiment. In the other compartment men slept, in contact with clothing, sheets, linen soiled with blood or vomit

CAMP LAZEAR



THE HUT AT CAMP LAZEAR

from yellow-fever patients. These experiments went on for 21 days. The men took no harm. When they had thus disproved the old belief that the fever can be transmitted by contagion, they exposed themselves to the mosquitoes, and all of them got the fever.

Thus, by 1901, the case against the mosquito was complete. As *Anopheles maculipennis* conveys malaria from man to man, so *Stegomyia calopus* conveys yellow fever from man to man. Therefore, to keep down malaria and yellow fever, keep down these mosquitoes. The eggs are laid on stagnant water: "ponds, swamps, puddles, roadside ditches, tanks, cisterns; and all such chance receptacles of rain-water as rain-barrels, pots and pans and broken bottles and old biscuit-tins—all the rubbish of the backyard." The larvæ live in the water, coming to the surface to breathe through their air-tubes. It is easy, therefore, to deal with them. "Pools and ditches are drained, or stocked with minnows, or filmed with kerosene to kill the larvæ; broken crockery and the like *débris* are carted away; cisterns and wells and rain-barrels are covered; everywhere, the surface-soil is tidied up; and all collections of stagnant water are cleared out."

By this labour, much of it unskilled, we know what great victories have been won over malaria

and yellow fever, not only in the Panama Zone, but in all parts of the world. To the victory over malaria, Greece and Italy and Egypt and Africa bear witness: for the victory over yellow fever, we may be content with the magnificent record of General Gorgas's work in Havana:

"Commencing in February, 1901, orders were issued that every suspected case of yellow fever should be screened with wire gauze at the public expense, so as to render the room or rooms mosquito-proof. All mosquitoes in the infected house and in contiguous houses were destroyed. After the middle of February, 100 men were employed in carrying out the destruction of the mosquito-larvæ in their breeding places, putting oil in the cesspools of all houses, clearing the streams, draining pools, and oiling the larger bodies of water. Up to June, quarantine was enforced, together with disinfection of the house and fomites (bedding, etc.). After that, however, rigid quarantine of the patient was stopped, and disinfection of fabrics and clothing ceased. It was merely required that the patient should be reported, his house placarded and screened, and a guard placed over each case, to report how general sick-room sanitation was carried out, to see that the screen-door communicating with the screened part of the house was kept properly closed, and to see that communication with the sick-room was not too free, four or five non-immunes only being allowed in.

"By the end of September, the last focus of the disease had been got rid of. . . . For the first time in 150 years, Havana has been free from

yellow fever."—Hewlett, *The Practitioner*, May, 1902.

DEATHS IN HAVANA FROM YELLOW FEVER.

Year.	Deaths.	Year.	Deaths.	Year.	Deaths.	Year.	Deaths.
1871	991	1881	485	1891	356	1901	18
1872	575	1882	729	1892	357	1902	0
1873	1,244	1883	849	1893	496	1903	0
1874	1,425	1884	511	1894	382	1904	0
1875	1,001	1885	165	1895	553		
1876	1,619	1886	167	1896	1,282		
1877	1,374	1887	532	1897	858		
1878	1,559	1888	468	1898	136		
1879	1,444	1889	303	1899	103		
1880	645	1890	308	1900	310		

There is not space, under the conditions of this book, to give more instances of the value of Pasteur's method. Many, perforce, have been left out: the work of Flexner on cerebro-spinal fever and on epidemic infantile paralysis, the work of Metchnikoff on arterio-sclerosis, Ehrlich on syphilis, Bruce on sleeping sickness, Leishman on kala-azar, Rogers on dysentery—these, and many more. Leprosy, relapsing fever, epidemic enteritis, oral sepsis, ankylostomiasis, general paralysis of the insane—it is Pasteur who decided how they should be studied.

His everlasting place in Science is high above the making of discoveries. He gave men a new system of scientific thought, and power to explore

the "kingdom of infinitely small things." Therefore he still is in authority over the innumerable purposes and uses of bacteriology. We trace his influence, to begin with—we must begin somewhere—in the manufacture of nitrates, the purification of sewage, the fertilising of soil, and the preservation of food: and, more immediately, in the silk-trade, and in the colossal industries of wine-making, vinegar-making, and brewing.

Again, we trace it in a thousand affairs of sanitation and of public health: but no room is left here to write of these.

Again, it is present in the study of the infective diseases of animals. These diseases have been investigated, during the past thirty years, as they never were before, by methods which are, ultimately, from him: and much of the fight against them is on lines laid down by him. Examples which come first to mind are the mallein test for glanders in horses, the tuberculin test for tuberculosis in cattle, and the protective use of tetanus-antitoxin for horses. Add to these the protective treatments against rinderpest and contagious pleuro-pneumonia in cattle, and the present researches into epizöotic abortion: and the work of Copeman on distemper, and of Nuttall on malignant jaundice of dogs.

But the advantage of these and the like researches

does not stop at saving the lives of animals, and profiting or pleasing their owners. It is doing more than that: it is bringing veterinary practice into union with medical and surgical practice. Every year, in this and other countries, the veterinary art is becoming more scientific, less of a craft, and more of a learned profession. Thirty years ago, this levelling up of the study of animal diseases to the study of human diseases was not possible, was hardly imaginable: and it is Pasteur, more than anyone else, who made it possible.

But the saving of the lives of animals is a small matter, compared to the gifts which come through him to man for the service, not of animals, but of man. In the present researches into human infective diseases, and in the present methods of dealing with them, where does he leave off? All the world over, wherever the science and art of medicine and surgery are, there his influence is, and his name is held in honour. *Vivit, regnat, imperat.* For he did more than make discoveries; he discovered how to make them.

That is why all nations are grateful to him. Take once more this one fact, that by the pursuit of his methods yellow fever has been stamped out, and the Panama Canal has been opened. In the whole history of science, there is no greater achievement. And what moves us, when we read of the work, is

not only the death of Lazear, nor even the saving of thousands of lives: it is the wonder of the work itself. Still, it is but one of many instances. From Pasteur's demonstration of the truth of "the germ-theory" have arisen other victories over disease, other improvements of the world's affairs: and more will arise in due time.

Here is the end of this book, written on the night of Friday, August 14, 1914. His country and ours, to-night, wait side by side, to suffer together. The greatness of that suffering, in death and mourning and poverty, none of us can measure: but come what may, our country is thankful that she saw her duty clear before her; and that she stands, now and henceforth, in friendship and in honour, hand in hand with France.

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